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Attorney Docket No.

210121.427C10

First Inventor or Application Identifier

Jiangchu Xu et al.

Title

COMPOSITIONS AND METHODS FOR THERAPY
AND DIAGNOSIS OF PROSTATE CANCER

Express Mail Label No.

EL487808240US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO:

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 202311. ☐ General Authorization Form & Fee Transmittal
(Submit an original and a duplicate for fee processing)2. ☒ Specification [Total Pages] **130**
(preferred arrangement set forth below)

- Descriptive Title of the Invention
- Cross References to Related Applications
- Statement Regarding Fed sponsored R & D
- Reference to Microfiche Appendix
- Background of the Invention

- Brief Summary of the Invention
- Brief Description of the Drawings (if filed)
- Detailed Description
- Claim(s)
- Abstract of the Disclosure

3. **16** Drawing(s) (35 USC 113) [Total Sheets] **1-12B**

4. Oath or Declaration [Total Pages]

- a. ☐ Newly executed (original or copy)
- b. ☐ Copy from a prior application (37 CFR 1.63(d))
(for continuation/divisional with Box 17 completed)
- i. ☐ DELETION OF INVENTOR(S)
Signed statement attached deleting
inventor(s) named in the prior
application,
see 37 CFR 1.63(d)(2) and 1.33(b)

5. ☐ Incorporation By Reference (useable if box 4b is checked) The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered to be part of the disclosure of the accompanying application and is hereby incorporated by reference therein.6. ☐ Microfiche Computer Program (Appendix)7. Nucleotide and Amino Acid Sequence Submission
(if applicable, all necessary)

- a. ☒ Computer-Readable Copy
- b. ☒ Paper Copy (identical to computer copy)
- c. ☒ Statement verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

8. ☐ Assignment Papers (cover sheet & document(s))9. ☐ 37 CFR 3.73(b) Statement ☐ Power of Attorney
(when there is an assignee)10. ☐ English Translation Document (if applicable)11. ☐ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations12. ☐ Preliminary Amendment13. ☒ Return Receipt Postcard14. ☐ Small Entity Statement(s) ☐ Statement filed in prior application, Status still proper and desired15. ☐ Certified Copy of Priority Document(s)
(if foreign priority is claimed)16. ☒ Other: Certificate of Express Mail

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information below and in a preliminary amendment

☐ Continuation ☐ Divisional ☒ Continuation-In-Part (CIP) of prior Application No.: Application filed 11/18/99

Prior application information: Examiner _____ Group / Art Unit _____

☐ Claims the benefit of Provisional (or foreign) Application No. _____

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TYPED or PRINTED NAME David J. Maki
SIGNATURE [Signature]

REGISTRATION NO. 31,392
Date January 14, 2000

COMPOSITIONS AND METHODS FOR THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

5

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Patent Application No. ____, filed November 18, 1999, which is a continuation-in-part of U.S. Patent Application No. 09/352,616, filed July 13, 1999, which is a continuation-in-part of U.S. Patent Application No. 09/288,946, filed April 9, 1999, which is a continuation-in-part of U.S. Patent Application No. 09/232,149, filed January 15, 1999, which is a continuation-in-part of U.S. Patent Application No. 09/159,812, filed September 23, 1998, which is a continuation-in-part of U.S. Patent Application No. 09/115,453, filed July 14, 1998, which is a continuation-in-part of U.S. Patent Application No. 09/030,607, filed February 25, 1998, which is a continuation-in-part of U.S. Patent Application No. 09/020,956, filed February 9, 1998, which is a continuation-in-part of U.S. Patent Application No. 08/904,804, filed August 1, 1997, which is a continuation-in-part of U.S. Patent Application No. 08/806,099, filed February 25, 1997.

TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to

that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

5 In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always
10 correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need
15 in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention
20 provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is
25 encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382,384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587 and 591; (b) sequences that hybridize to any of the foregoing sequences under moderately

stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586 and 588-590.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-551, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the

level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other
5 embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a
10 patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide. (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected
15 in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or
20 primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

25 BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

Figures 12A and B are the full-length cDNA (SEQ ID NO:591) and predicted amino acid (SEQ ID NO:592) sequences, respectively, for the clone P788P.

5 SEQ ID NO: 1 is the determined cDNA sequence for F1-13
SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12
SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
10 SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
15 SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
20 SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
25 SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63

SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
 SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
 SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
 SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
 5 SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
 SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
 SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
 SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
 SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
 10 SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
 SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
 SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
 SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
 SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861
 15 SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
 SEQ ID NO: 41 is the determined cDNA sequence for P5
 SEQ ID NO: 42 is the determined cDNA sequence for P8
 SEQ ID NO: 43 is the determined cDNA sequence for P9
 SEQ ID NO: 44 is the determined cDNA sequence for P18
 20 SEQ ID NO: 45 is the determined cDNA sequence for P20
 SEQ ID NO: 46 is the determined cDNA sequence for P29
 SEQ ID NO: 47 is the determined cDNA sequence for P30
 SEQ ID NO: 48 is the determined cDNA sequence for P34
 SEQ ID NO: 49 is the determined cDNA sequence for P36
 25 SEQ ID NO: 50 is the determined cDNA sequence for P38
 SEQ ID NO: 51 is the determined cDNA sequence for P39
 SEQ ID NO: 52 is the determined cDNA sequence for P42
 SEQ ID NO: 53 is the determined cDNA sequence for P47
 SEQ ID NO: 54 is the determined cDNA sequence for P49

SEQ ID NO: 55 is the determined cDNA sequence for P50

SEQ ID NO: 56 is the determined cDNA sequence for P53

SEQ ID NO: 57 is the determined cDNA sequence for P55

SEQ ID NO: 58 is the determined cDNA sequence for P60

5 SEQ ID NO: 59 is the determined cDNA sequence for P64

SEQ ID NO: 60 is the determined cDNA sequence for P65

SEQ ID NO: 61 is the determined cDNA sequence for P73

SEQ ID NO: 62 is the determined cDNA sequence for P75

SEQ ID NO: 63 is the determined cDNA sequence for P76

10 SEQ ID NO: 64 is the determined cDNA sequence for P79

SEQ ID NO: 65 is the determined cDNA sequence for P84

SEQ ID NO: 66 is the determined cDNA sequence for P68

SEQ ID NO: 67 is the determined cDNA sequence for P80

SEQ ID NO: 68 is the determined cDNA sequence for P82

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SEQ ID NO: 70 is the determined cDNA sequence for U1-3065

SEQ ID NO: 71 is the determined cDNA sequence for V1-3692

SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905

SEQ ID NO: 73 is the determined cDNA sequence for V1-3686

20 SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976

SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736

SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738

25 SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741

SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744

SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734

SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774

SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781

SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785

SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787

SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796

SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807

5 SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810

SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811

SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876

SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896

10 SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761

SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762

SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766

SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770

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15 SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772

SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297

SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309

SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278

SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288

20 SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283

SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304

SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

25 SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

5 SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

SEQ ID NO: 115 is the determined cDNA sequence for P89

SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92

SEQ ID NO: 118 is the determined cDNA sequence for P95

10 SEQ ID NO: 119 is the determined cDNA sequence for P98

SEQ ID NO: 120 is the determined cDNA sequence for P102

SEQ ID NO: 121 is the determined cDNA sequence for P110

SEQ ID NO: 122 is the determined cDNA sequence for P111

SEQ ID NO: 123 is the determined cDNA sequence for P114

15 SEQ ID NO: 124 is the determined cDNA sequence for P115

SEQ ID NO: 125 is the determined cDNA sequence for P116

SEQ ID NO: 126 is the determined cDNA sequence for P124

SEQ ID NO: 127 is the determined cDNA sequence for P126

SEQ ID NO: 128 is the determined cDNA sequence for P130

20 SEQ ID NO: 129 is the determined cDNA sequence for P133

SEQ ID NO: 130 is the determined cDNA sequence for P138

SEQ ID NO: 131 is the determined cDNA sequence for P143

SEQ ID NO: 132 is the determined cDNA sequence for P151

SEQ ID NO: 133 is the determined cDNA sequence for P156

25 SEQ ID NO: 134 is the determined cDNA sequence for P157

SEQ ID NO: 135 is the determined cDNA sequence for P166

SEQ ID NO: 136 is the determined cDNA sequence for P176

SEQ ID NO: 137 is the determined cDNA sequence for P178

SEQ ID NO: 138 is the determined cDNA sequence for P179

SEQ ID NO: 139 is the determined cDNA sequence for P185
 SEQ ID NO: 140 is the determined cDNA sequence for P192
 SEQ ID NO: 141 is the determined cDNA sequence for P201
 SEQ ID NO: 142 is the determined cDNA sequence for P204
 5 SEQ ID NO: 143 is the determined cDNA sequence for P208
 SEQ ID NO: 144 is the determined cDNA sequence for P211
 SEQ ID NO: 145 is the determined cDNA sequence for P213
 SEQ ID NO: 146 is the determined cDNA sequence for P219
 SEQ ID NO: 147 is the determined cDNA sequence for P237
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 SEQ ID NO: 156 is the determined cDNA sequence for P264
 SEQ ID NO: 157 is the determined cDNA sequence for P266
 20 SEQ ID NO: 158 is the determined cDNA sequence for P270
 SEQ ID NO: 159 is the determined cDNA sequence for P272
 SEQ ID NO: 160 is the determined cDNA sequence for P278
 SEQ ID NO: 161 is the determined cDNA sequence for P105
 SEQ ID NO: 162 is the determined cDNA sequence for P107
 25 SEQ ID NO: 163 is the determined cDNA sequence for P137
 SEQ ID NO: 164 is the determined cDNA sequence for P194
 SEQ ID NO: 165 is the determined cDNA sequence for P195
 SEQ ID NO: 166 is the determined cDNA sequence for P196
 SEQ ID NO: 167 is the determined cDNA sequence for P220

SEQ ID NO: 168 is the determined cDNA sequence for P234

SEQ ID NO: 169 is the determined cDNA sequence for P235

SEQ ID NO: 170 is the determined cDNA sequence for P243

SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1

5 SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1

SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2

SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6

SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13

SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

10 SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-4736

SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-4741

15 SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-4781

SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-4787

20 SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876

25 SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896

SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761

SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762

SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766

SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771

SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772

SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309

5 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278

SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288

SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283

SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304

SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296

10 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280

SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd

SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con

SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev

SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd

15 SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev

SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev

SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd

SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev

20 SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd

SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev

SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd

SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev

SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev

25 SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd

SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev

SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEQ ID NO: 224 is the determined cDNA sequence for P510S

SEQ ID NO: 225 is the determined cDNA sequence for P703DE5

SEQ ID NO: 226 is the determined cDNA sequence for 9-A11

SEQ ID NO: 227 is the determined cDNA sequence for 8-C6

SEQ ID NO: 228 is the determined cDNA sequence for 8-H7

SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

5 SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14

SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23

SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24

SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25

SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30

10 SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34

SEQ ID NO: 236 is the determined cDNA sequence for PTPN35

SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36

SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38

SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39

15 SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40

SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41

SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45

SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46

20 SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51

SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56

SEQ ID NO: 247 is the determined cDNA sequence for PTPN64

SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65

SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67

25 SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76

SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84

SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85

SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86

SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87

SEQ ID NO: 255 is the determined cDNA sequence for JP1PN88

SEQ ID NO: 256 is the determined cDNA sequence for JP1F1

SEQ ID NO: 257 is the determined cDNA sequence for JP1F2

SEQ ID NO: 258 is the determined cDNA sequence for JP1C2

5 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1

SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

SEQ ID NO: 262 is the determined cDNA sequence for JP1A4

SEQ ID NO: 263 is the determined cDNA sequence for JP1F5

10 SEQ ID NO: 264 is the determined cDNA sequence for JP1E6

SEQ ID NO: 265 is the determined cDNA sequence for JP1D6

SEQ ID NO: 266 is the determined cDNA sequence for JP1B5

SEQ ID NO: 267 is the determined cDNA sequence for JP1A6

SEQ ID NO: 268 is the determined cDNA sequence for JP1E8

15 SEQ ID NO: 269 is the determined cDNA sequence for JP1D7

SEQ ID NO: 270 is the determined cDNA sequence for JP1D9

SEQ ID NO: 271 is the determined cDNA sequence for JP1C10

SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12

20 SEQ ID NO: 274 is the determined cDNA sequence for JP1E12

SEQ ID NO: 275 is the determined cDNA sequence for JP1D11

SEQ ID NO: 276 is the determined cDNA sequence for JP1C11

SEQ ID NO: 277 is the determined cDNA sequence for JP1C12

SEQ ID NO: 278 is the determined cDNA sequence for JP1B12

25 SEQ ID NO: 279 is the determined cDNA sequence for JP1A12

SEQ ID NO: 280 is the determined cDNA sequence for JP8G2

SEQ ID NO: 281 is the determined cDNA sequence for JP8H1

SEQ ID NO: 282 is the determined cDNA sequence for JP8H2

SEQ ID NO: 283 is the determined cDNA sequence for JP8A3

SEQ ID NO: 313 is the determined cDNA sequence for P710P

SEQ ID NO: 314 is the determined cDNA sequence for P767P

SEQ ID NO: 315 is the determined cDNA sequence for P768P

SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes

5 SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5

SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5

SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26

SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26

SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23

10 SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23

SEQ ID NO: 332 is the determined full length cDNA sequence for P509S

SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)

SEQ ID NO: 334 is the determined cDNA sequence for P714P

15 SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)

SEQ ID NO: 336 is the predicted amino acid sequence for P705P

SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

SEQ ID NO: 338 is the amino acid sequence of the peptide p5

SEQ ID NO: 339 is the predicted amino acid sequence of P509S

20 SEQ ID NO: 340 is the determined cDNA sequence for P778P

SEQ ID NO: 341 is the determined cDNA sequence for P786P

SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

25 SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

5 SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

10 SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

15 SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

20 SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

25 SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

5 SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

10 SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

15 SEQ ID NO:389 is the cDNA sequence for 23379

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

20 SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

25 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.
SEQ ID NO:405 is the cDNA sequence for 22551.
SEQ ID NO:406 is the cDNA sequence for 22552.
SEQ ID NO:407 is the cDNA sequence for 22553.
5 SEQ ID NO:408 is the cDNA sequence for 22558.
SEQ ID NO:409 is the cDNA sequence for 22562.
SEQ ID NO:410 is the cDNA sequence for 22565.
SEQ ID NO:411 is the cDNA sequence for 22567.
SEQ ID NO:412 is the cDNA sequence for 22568
10 SEQ ID NO:413 is the cDNA sequence for 22570.
SEQ ID NO:414 is the cDNA sequence for 22571.
SEQ ID NO:415 is the cDNA sequence for 22572.
SEQ ID NO:416 is the cDNA sequence for 22573.
SEQ ID NO:417 is the cDNA sequence for 22573.
15 SEQ ID NO:418 is the cDNA sequence for 22575.
SEQ ID NO:419 is the cDNA sequence for 22580
SEQ ID NO:420 is the cDNA sequence for 22581.
SEQ ID NO:421 is the cDNA sequence for 22582.
SEQ ID NO:422 is the cDNA sequence for 22583.
20 SEQ ID NO:423 is the cDNA sequence for 22584.
SEQ ID NO:424 is the cDNA sequence for 22585.
SEQ ID NO:425 is the cDNA sequence for 22586.
SEQ ID NO:426 is the cDNA sequence for 22587.
SEQ ID NO:427 is the cDNA sequence for 22588.
25 SEQ ID NO:428 is the cDNA sequence for 22589.
SEQ ID NO:429 is the cDNA sequence for 22590.
SEQ ID NO:430 is the cDNA sequence for 22591.
SEQ ID NO:431 is the cDNA sequence for 22592.
SEQ ID NO:432 is the cDNA sequence for 22593.

SEQ ID NO:433 is the cDNA sequence for 22594.
 SEQ ID NO:434 is the cDNA sequence for 22595.
 SEQ ID NO:435 is the cDNA sequence for 22596.
 SEQ ID NO:436 is the cDNA sequence for 22847.
 5 SEQ ID NO:437 is the cDNA sequence for 22848.
 SEQ ID NO:438 is the cDNA sequence for 22849.
 SEQ ID NO:439 is the cDNA sequence for 22851.
 SEQ ID NO:440 is the cDNA sequence for 22852.
 SEQ ID NO:441 is the cDNA sequence for 22853.
 10 SEQ ID NO:442 is the cDNA sequence for 22854.
 SEQ ID NO:443 is the cDNA sequence for 22855.
 SEQ ID NO:444 is the cDNA sequence for 22856.
 SEQ ID NO:445 is the cDNA sequence for 22857.
 SEQ ID NO:446 is the cDNA sequence for 23601.
 15 SEQ ID NO:447 is the cDNA sequence for 23602.
 SEQ ID NO:448 is the cDNA sequence for 23605.
 SEQ ID NO:449 is the cDNA sequence for 23606.
 SEQ ID NO:450 is the cDNA sequence for 23612.
 SEQ ID NO:451 is the cDNA sequence for 23614.
 20 SEQ ID NO:452 is the cDNA sequence for 23618.
 SEQ ID NO:453 is the cDNA sequence for 23622.
 SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
 SEQ ID NO:455 is the cDNA sequence for LIM protein.
 SEQ ID NO:456 is the cDNA sequence for a known gene.
 25 SEQ ID NO:457 is the cDNA sequence for a known gene.
 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
 SEQ ID NO:459 is the cDNA sequence for 23045.
 SEQ ID NO:460 is the cDNA sequence for 23032.
 SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

5 SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

10 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

15 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P

20 SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

25 SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

SEQ ID NO: 552 is an extended cDNA sequence for P712P.

5 SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

SEQ ID NO: 570 is the determined cDNA sequence for a splice variant of P776P referred to as contig 6.

10 SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

15 SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

20 SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

DETAILED DESCRIPTION OF THE INVENTION

25 As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune

system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs. 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586 and 588-590.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of

a prostate-specific protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The term “variants” also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be “identical” if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references. Dayhoff, M.O. (1978) A model of evolutionary change in

proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide

sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns

containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a

polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

5 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

10 Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591. Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

15 Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA 2*:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such
20 that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

25 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs

that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone, and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-, methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors. Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In

other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine, and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide

as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S.

Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

5 The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

10 Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med* , 336:86-91, 1997).

15 Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional
20 exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

25 In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of

the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen

without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from
5 related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific polypeptide or polynucleotide is present within a delivery vehicle, such as a
10 microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example,
20 T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in
25 activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Prostate-specific protein-specific T

cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral,

nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines

(e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; *see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or

antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate-specific polypeptide, DNA (naked or within a plasmid

vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors

specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous),

intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of

other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or

polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates

a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 μ g/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A

level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy

tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A⁺ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64×10^7 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3×10^6 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full

length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H₂O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike"

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A⁺ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905,

are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS. 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively).

Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS. 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS. 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA)

demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the

hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was

minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-

17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

5 The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

10 Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

15 The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal

tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO:

225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The

determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331,

respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked

to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also

led to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction

enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different
5 adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d)
10 unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed
15 sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was
20 then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven
25 further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JTPN46

(SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

5 Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365. The full length cDNA sequence of the clone of SEQ ID NO: 362 (referred to as P788P) is shown in Figure 12A, with the corresponding predicted amino acid being shown in Figure 12B.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common, suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6 1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the

presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 μ g/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6×10^6 cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5×10^5 /ml) were restimulated with 2.5×10^6 /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3×10^6 /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION

WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between

immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ -interferon ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10⁴ fibroblasts in the presence of 3 μ g/ml human β_2 -microglobulin and 1 μ g/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ -

interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES

IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced to express P501S and CD80, CD8⁺ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (⁵¹Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

5 The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically
10 recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized
15 subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as
20 well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures
25 derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 µg/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was

demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

EXAMPLE 11

5 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

20 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- γ ELISPOT analysis as described above. Using a panel of

HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 µg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8⁺ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8⁺ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8⁺ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-γ ELISPOT assays against these A2Kb targets transduced with the “library” of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-γ assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL.

Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8⁺ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

BY MICROARRAY ANALYSIS

25 This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced.

- 5 Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142 2. bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang

showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed

genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II
Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus,

Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are

provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known

432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones

are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a) Expression in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site.

AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to aggregation of the recombinant

protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot

with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 μ l of Fugene reagent was diluted into 100 μ l of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 μ g of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 μ l of GenePorter was diluted in 500 μ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 μ g of plasmid DNA that was diluted in 500 μ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS

to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The

results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (μg/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 μg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-

transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and “native” P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum,

kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3

and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

b) Preparation and Characterization of Antibodies against P503S

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells

were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

c) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM technology at Immgenics

Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk^{-/-} cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected

with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO. 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically,

Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the

longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science*

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid
5 sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407,
10 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).
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2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207,
20 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587, or a complement of any of the foregoing polynucleotide sequences.

25 3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586 and 588-590.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587.

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7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

14. A fusion protein comprising at least one polypeptide according to claim 1.

15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to claim 14.

19. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- (d) a fusion protein according to claim 14; and

- (e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to any one of claims 11-13;
(d) a fusion protein according to claim 14; and
(e) a polynucleotide according to claim 18.

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant induces a predominantly Type I response

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591, and thereby inhibiting the development of a cancer in the patient.

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42 A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587 and 591, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

56. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and

(b) a detection reagent comprising a reporter group.

57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin

59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-

specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-361, 363-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572 and 587.

62. A diagnostic kit, comprising:

- (a) an oligonucleotide according to claim 61; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim 10.

COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF
PROSTATE CANCER

ABSTRACT OF THE DISCLOSURE

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

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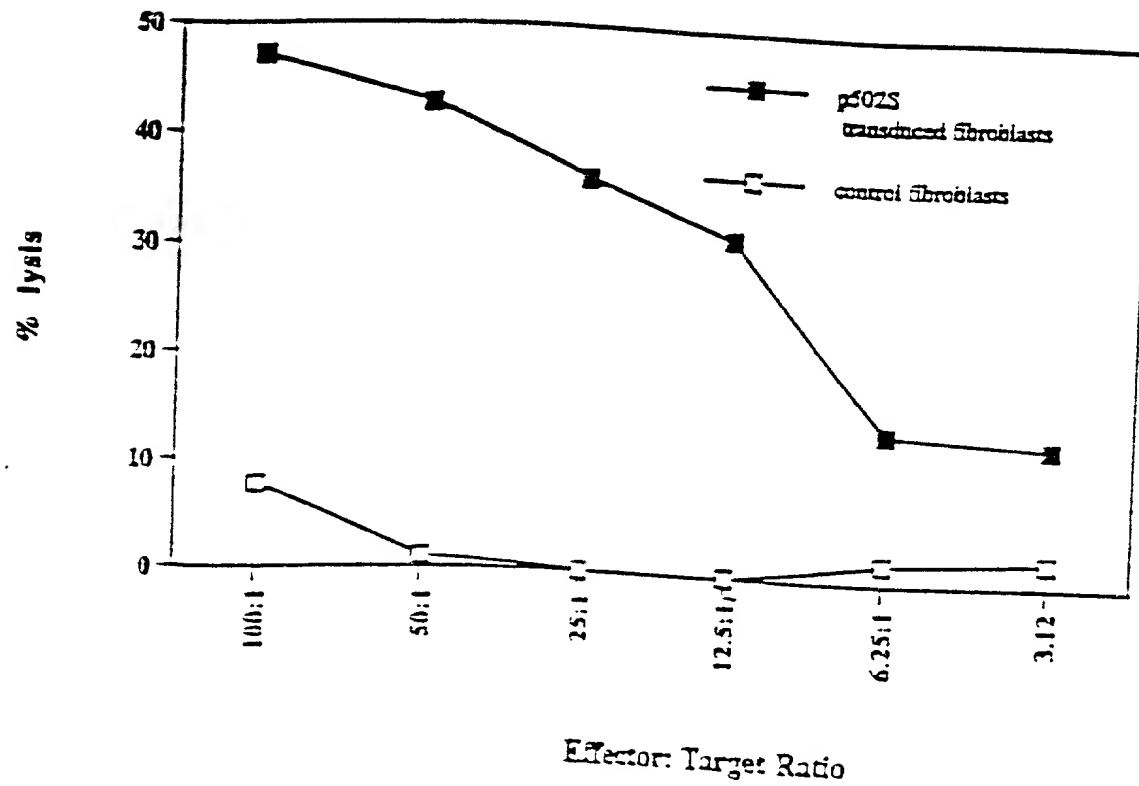


Fig. 1

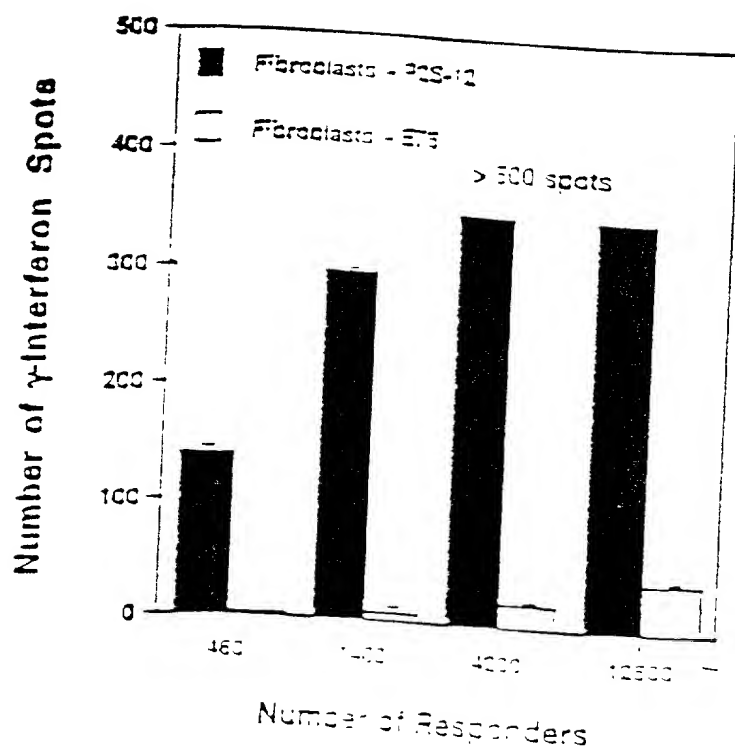


Fig. 2A

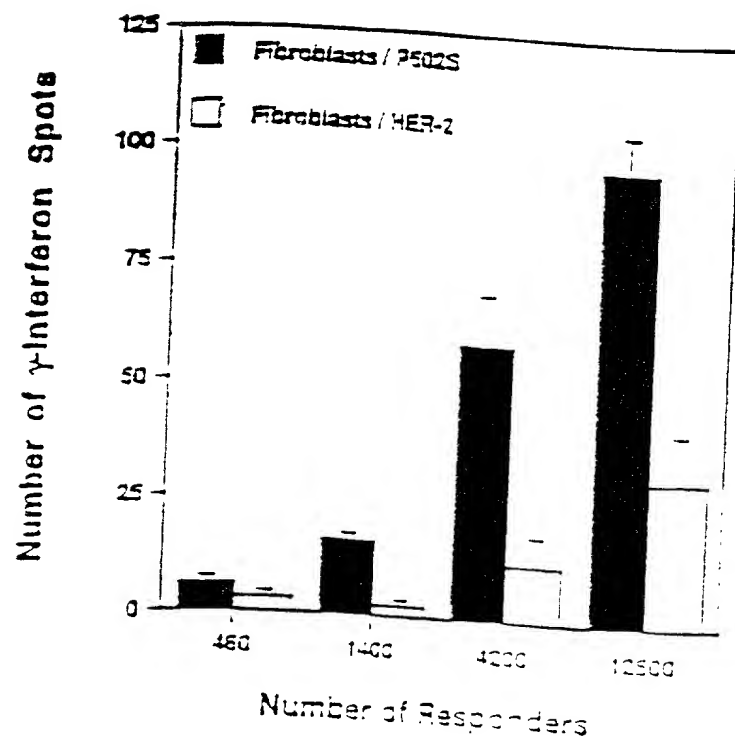


Fig. 2B

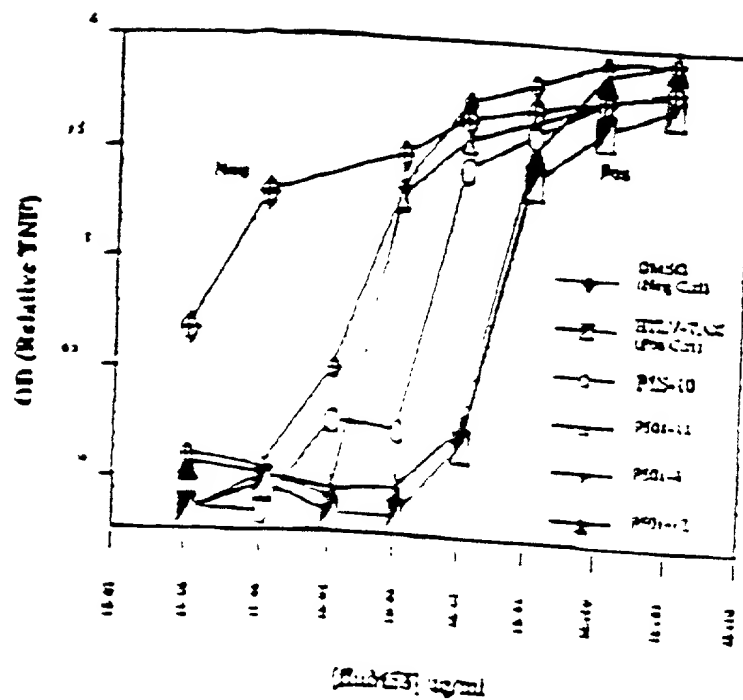


Fig. 3

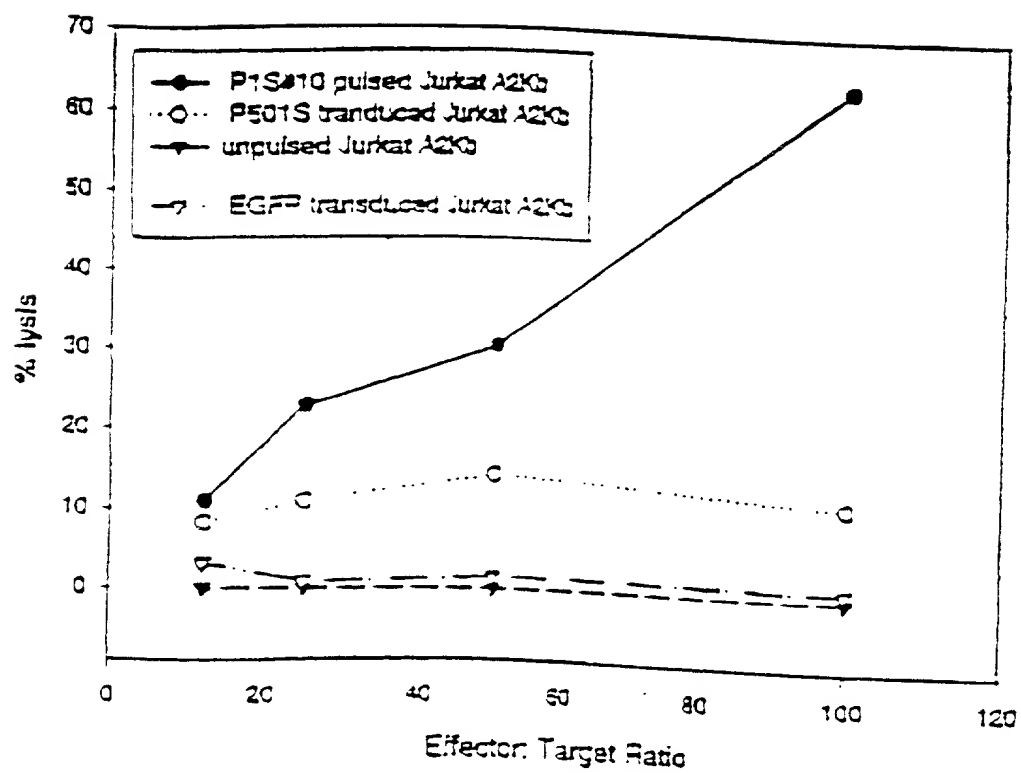


Fig. 4

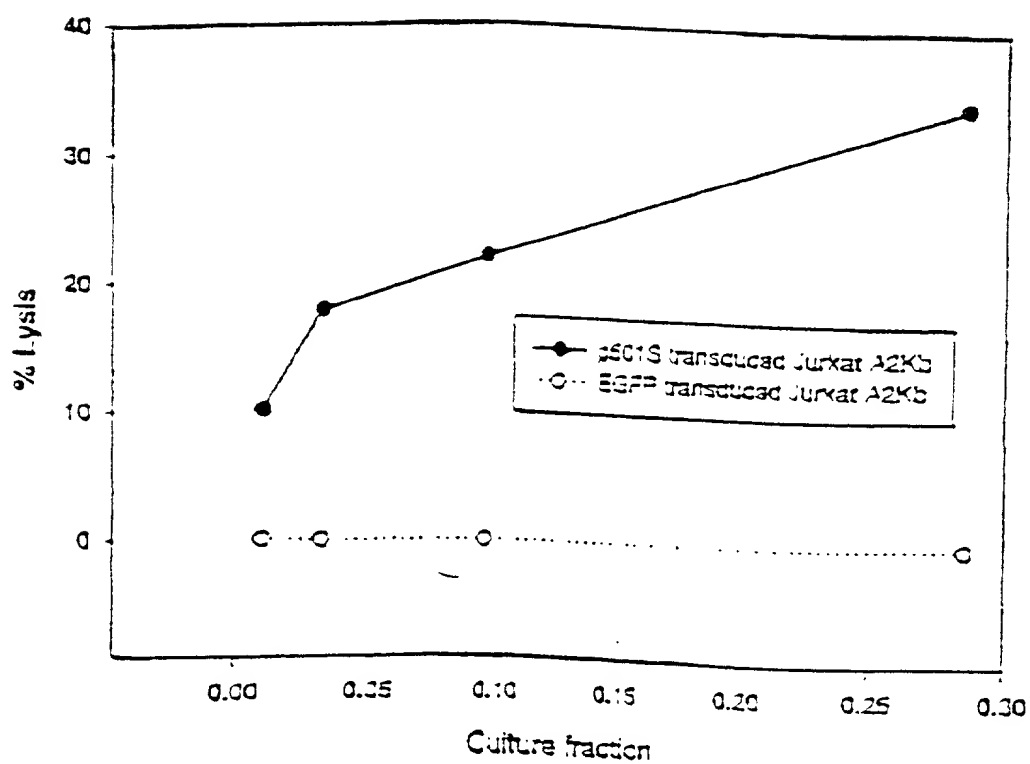


Fig. 5

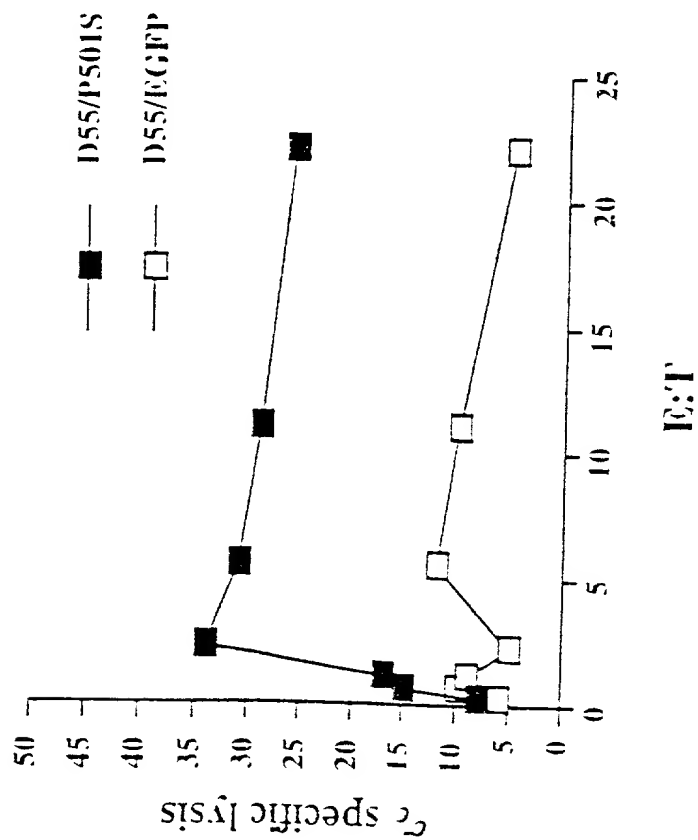


Fig. 6A

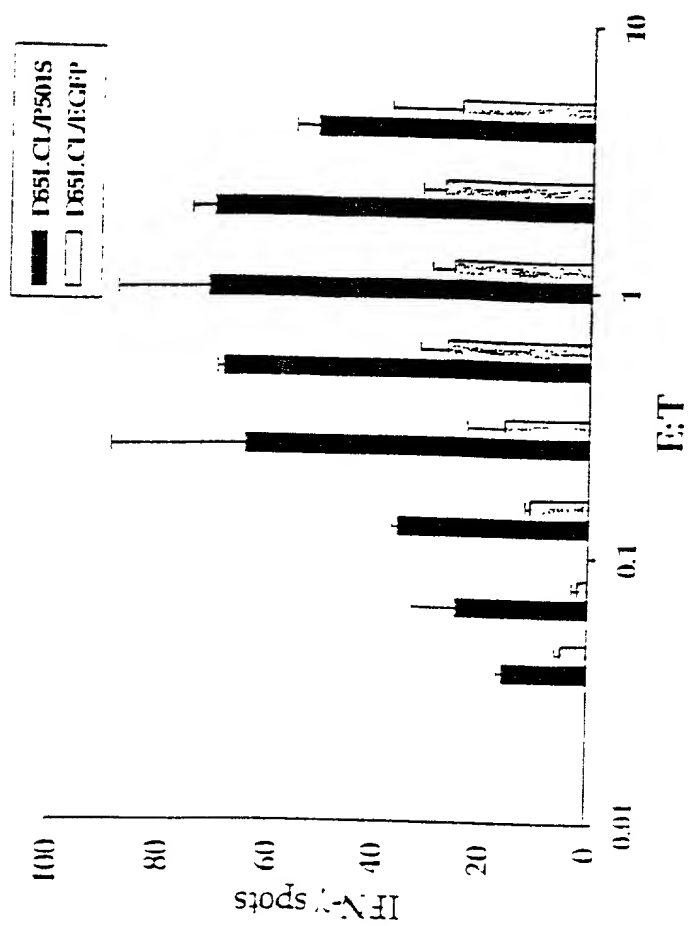
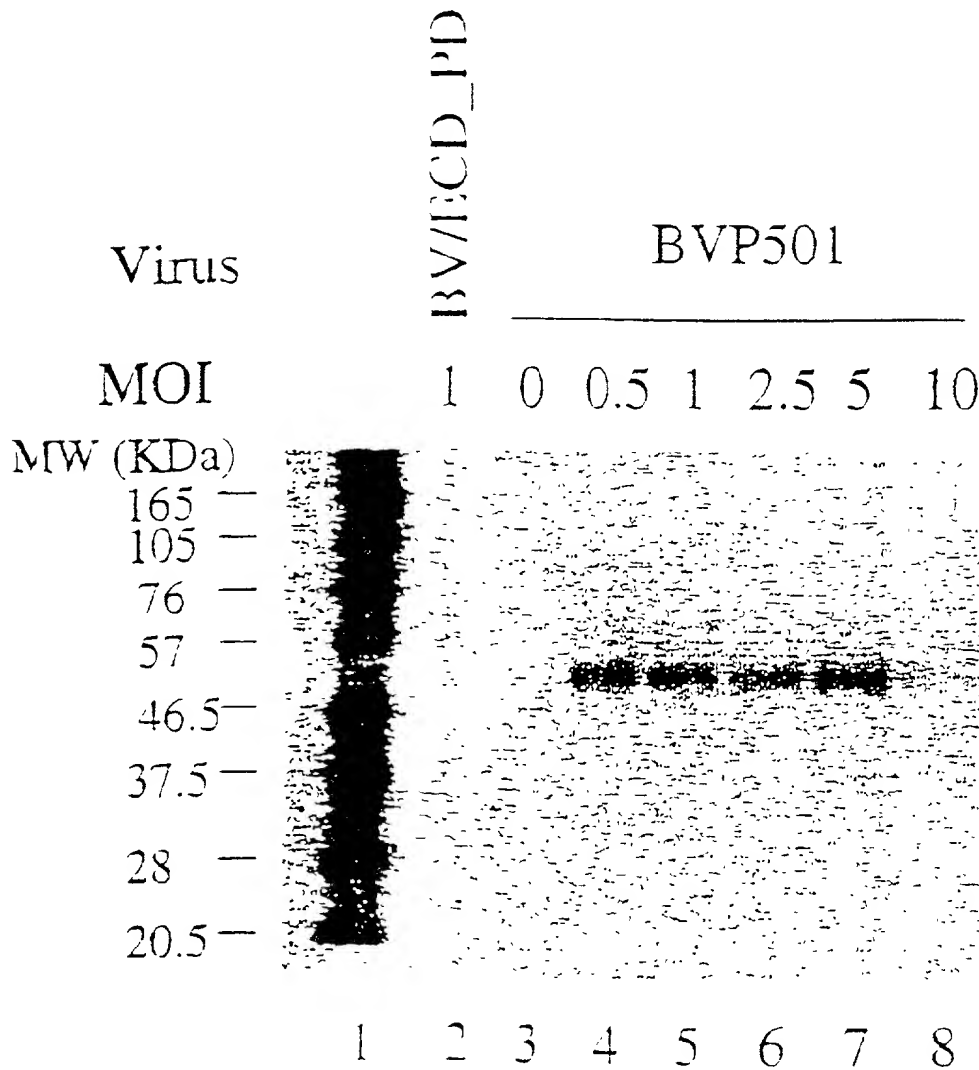


Fig. 6B

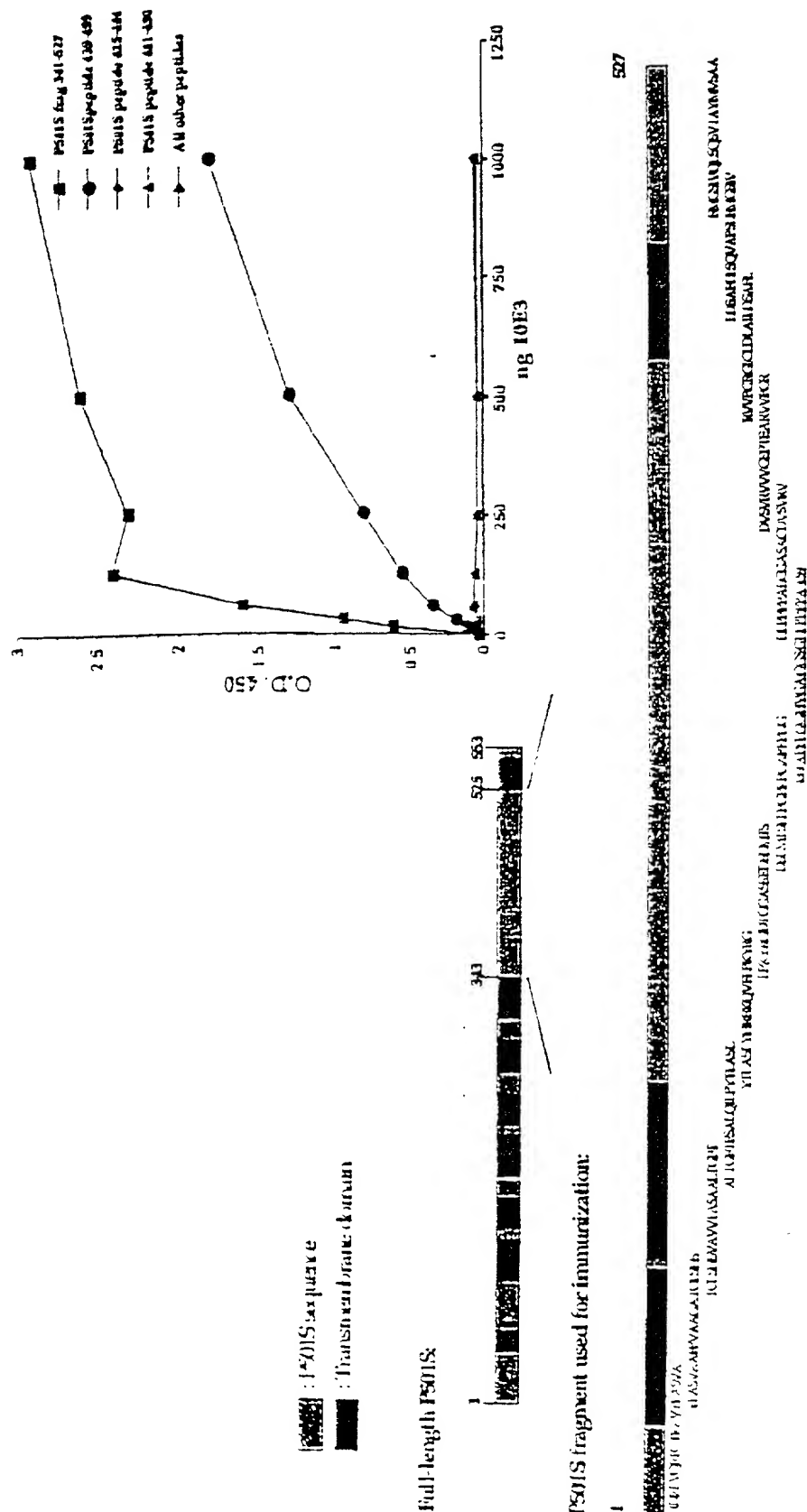
Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

Figure 8. Mapping of the epitope recognized by 10E3-G4-D3



7

Figure 1. Schematic of P501S with predicted transmembrane, cytoplasmic, and extracellular regions

MYQRLWVSRLRIKK AQLLLVNLITGLEVCI AAGIT VVPPLILEVGVERKEM TNVLGIGPVILGLYCVPLIGSAS
DIWRCRYGRRRP FIWALSIGILLISLFLPRAGWL AGLICPDPRPLE LALLGVGLIDFCGGQVCFITPL
FALLSDLFRDPDHCRQ AYSVYAFMISLGGCI QNIIPAI DVIDTSALAPYLGTQIEE
CLFGILLITFLTCVAAITLV AEEAAICPTEPAEGISAPISPHCCPC RARIAFRNLGAILPRL
IQLCCHMPRTLRR LPVAELCSWMALNITFLFYIDP YGEGLYQGVPRAPPGTEARRHIYDEGVYR
MGSLGLFLQCAISLVFSLVM DRIVQREFGTRAVVLAS VAAFPVAAAGATCLSHSVAVVTA SAA
LTGFIIFSALQILPYTLASLY HREKQVFLPKYRGDTGGASSEDSIMTSFLPGPKPGAPFPNGHIVGAGGSGL
LPPPPALCGASACDVSVRVVVGEPTEARVVPCRG ICLDPLAILDSAFLLSQVAPSLF MGSIVQLSQS
VTAYMVSAAAGLGLVAIFYAT QVVFDKSDIAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold sequence**: Predicted extracellular domain;
Italic sequence: Predicted intracellular domain. Sequence in bold/underlined: used to generate polyclonal rabbit serum

Localization of domains predicted using IMMTOPI (G.E. Tusnady and I. Simon (1998) Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to topology Prediction. *J Mol Biol.* 283, 489-506.

Genomic Map of (5) Corixa Candidate Genes

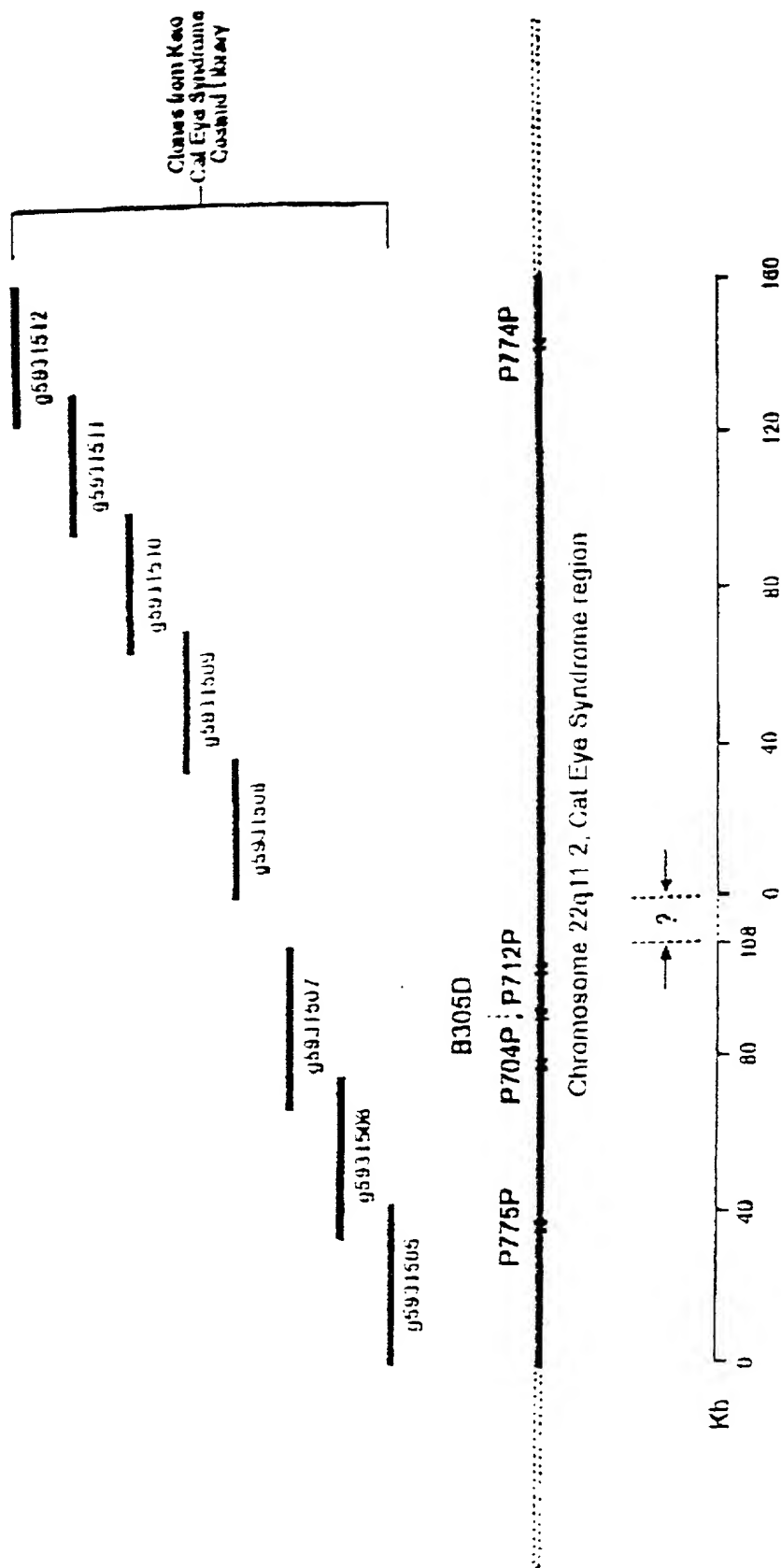


Fig. 10

11

FIGURE 4. Elisa assay of rabbit polyclonal antibody specificity

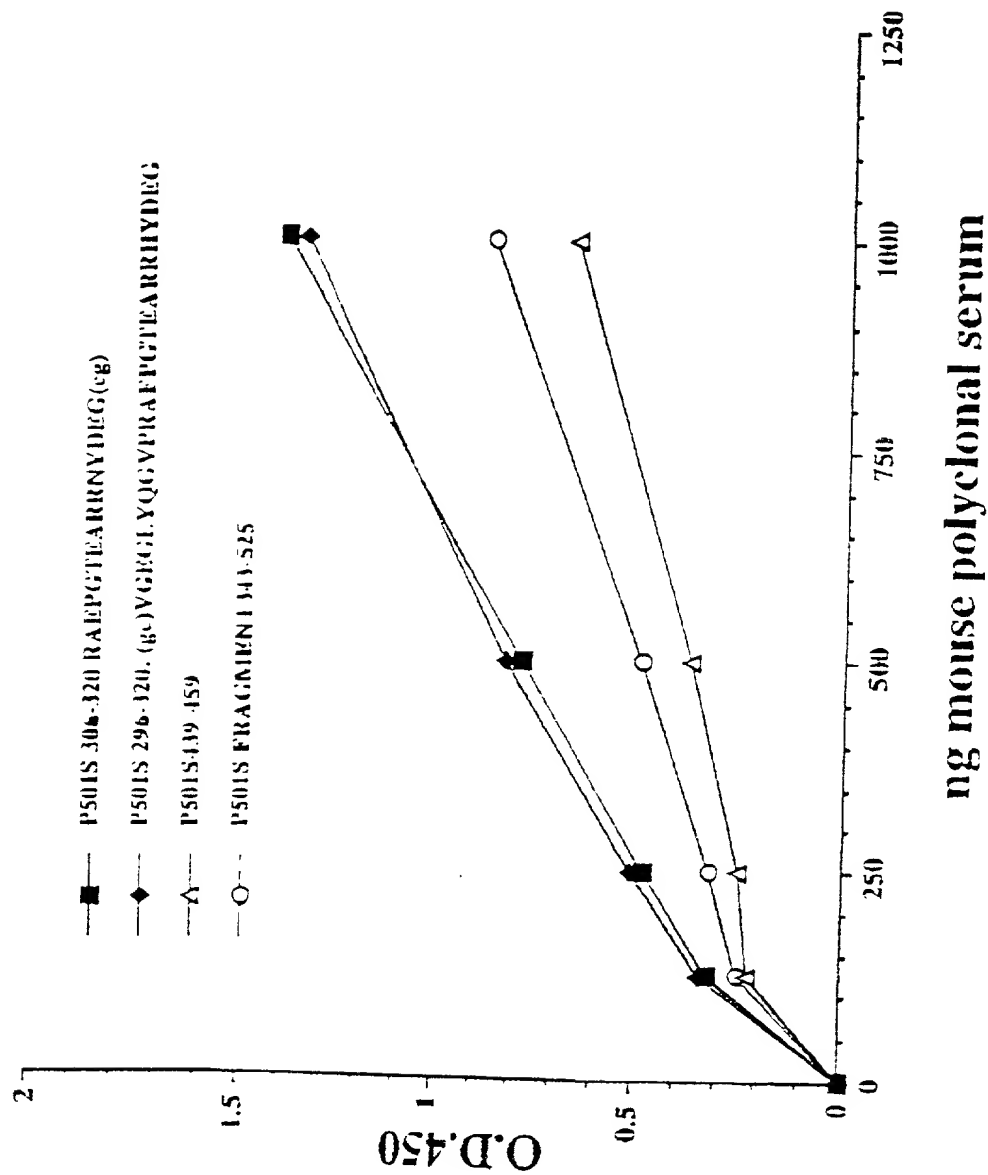


Fig. 11

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 AATGTGTGCAAGTGTGGCTATGCCAGAGCCAGCACATGGAAGGCACCCAGATCAACCAAAGTGAGAAAT 280
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 360 370 380 390 400 410 420
 GAAGAAAGGGAAGTATATACGTCTGTCTTGCAGACACGGACGCGGAAATCCTTTACGAGCTGCTGACCCAG 420
 CACTGGCACCTGAAAACACCCAACTGGTCAATTTCTGTGACCGGGGGCGCCAAGAACTTCGCCCTGAAGC 490
 CGCGCATGCGCAAGATCTTCAGCCGGCTCATCTACATCGCGCAGTCCAAAGGTGCTTGGATTCTCACGGG 560
 AGGCACCCATTATGGCCTGACGAAGTACATCGGGGAGGTGGTGAGAGATAACACCATCAGCAGGAGTTCA 630
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Fig. 12A

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2460	2470	2480	2490	2500	2510	2520
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2810	2820	2830	2840	2850	2860	2870
<p>GCACCTTCACTGGGAATGAGTCCAAGCCACTGTGTGTGGAGCTGGATGAGCACAACCTGCCCGGGTTCCC 2870</p> <p>CGAGTGGATCACCATCCCCCTGGTGTGCATCTACATGTTATCCACCAACATCCTGCTGGTCAACCTGCTG 2940</p> <p>GTCGCCATGTTTGGCTACACGGTGGGCACCGTCCAGGAGAACAATGACCAGGTCTGGAAGTTCAGAGGT 3010</p> <p>ACTTCTGGTGCAGGAGTACGCGAGCCGCTCAATATCCCTTCCCTTCATCGTCTTCGCTTACTTCTA 3080</p> <p>CATGGTGGTGAAGAAGTGCTTCAAGTGTGCTGCAAGGAGAAAAACATGGAGTCTTCTGTCTGCTGTTTC 3150</p>						
3160	3170	3180	3190	3200	3210	3220
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Fig. 12B

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Jiangchun Xu, Davin C. Dillon, Jennifer L. Mitcham ,
Susan Louise Harlocker, Jiang Yuqui, Steven G. Reed,
Michael Kalos, Gary Fanger, Mark Retter, John Solk
and Craig Day
Filed : January 14, 2000
For : COMPOSITIONS AND METHODS FOR THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

Docket No. : 210121.427C10

Date : January 14, 2000

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

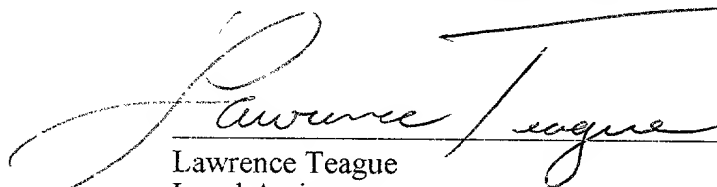
DECLARATION

Sir:

I, Lawrence Teague, in accordance with 37 C.F.R. § 1.821(f) do hereby declare that, to the best of my knowledge, the content of the paper entitled "Sequence Listing" and the computer readable copy contained within the floppy disk are the same

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated this 14th day of January, 2000.


Lawrence Teague
Legal Assistant

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SEQUENCE LISTING

<110> Xu, Jiangchun
 Dillon, Davin C.
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 Harlocker, Susan Louise
 Jiang Yuqui
 Reed, Steven G.
 Kalos, Michael
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 Solk, John
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ttcatggctg	ttggagcaat	agaaccccag	tlctacgagc	tgctgatcaa	aggacttggg	120
ctaaagtctg	atgaacttcc	caatcagatg	agcatggatg	attggccaga	aatgaagaag	180
aagtttgcag	atgtatttgc	aaagaagacg	aaggcagagt	gggtgcaaat	ctttgacggc	240
acagatgcct	gtgtgactcc	ggttctgact	tttgaggagg	ttgttcatca	tgatcacaa	300
aaggaacggg	gctcgtttat	caccagttag	gagcaggacg	tgagcccccg	ccctgcacct	360
ctgctgttaa	acaccccagc	catcccttct	ttcaaaagg	atccactagt	tctagaagcg	420
gccgccaccg	cggtggagct	ccagcttttg	ttccctttag	tgagggttaa	ttgcgcgctt	480
ggcgtaatca	tggtcatagc	tgtttcctgt	gtgaaattgt	tatccgctca	caattcccc	540
aacatacgag	ccggaacata	aaagtgttaag	cctgggggtgc	ctaattgantg	agctaactcn	600
cattaattgc	gttgcgctca	ctgcccgctt	tccagtcggg	aaaactgtcg	tgccactgcn	660
ttantgaatc	ngccaccccc	cgggaaaagg	cggttgcn	ttgggcctct	tccgcttccc	720
tcgctcattg	atcctngcnc	ccggtcttcg	gctgcggnga	acggttcaact	cctcaaaggc	780
ggtntnccgg	ttatccccaa	acnggggata	ccngga			816

<210> 3
 <211> 773
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(773)
 <223> n = A,T,C or G

<400> 3

cttttgaaag	aagggatggc	tgggggtgtt	aacagcagag	gtgcagggcg	ggggctcacg	60
tcctgctcct	cactgggtgat	aaacgagccc	cgttccttgt	tgtgatcatg	atgaacaacc	120
tcctcaaaag	tcagaaccgg	agtcacacag	gcattctgtc	cgtcaaagat	ttgacaccac	180
tctgccttcg	tcttctttgc	aaatacatct	gcaacttctt	tcttcatttc	tggccaatca	240
tccatgctca	tctgattggg	aagttcatca	gacttttagtc	canntccttt	gatcagcagc	300
tcgtagaact	ggggttctat	tgtctcaaca	gccatgaatt	ccccatctgc	tgtcctgtaa	360
gtcgatataga	aaggtgctcc	accatccaac	atgttctgtc	ctcgaggggg	ggcccggtag	420
ccaattcgcc	ctatantgag	tcgtattacg	cgcgctcact	ggccgctcgt	ttacaacgtc	480
gtgactggga	aaaccctggg	cgtaaccaac	ttaatcgctt	tgcagcacat	ccccctttcg	540
ccagctgggc	gtaatancca	aaaggccccg	accgatcgcc	cttccaacag	ttgcgcacct	600
gaatgggnaa	atgggacccc	cctgttaacc	cgcattnaac	ccccgcnggg	tttngttgtt	660
acccccacnt	nnaccgctta	cactttgcca	ggcgcttanc	ggccgctccc	tttncctttt	720
cttcccttcc	tttncncncn	ctttcccccg	gggtttcccc	cntcaaacc	cna	773

<210> 4
 <211> 828
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(828)
 <223> n = A,T,C or G

<400> 4

cctcctgagt	cctactgacc	tgtgctttct	ggtgtggagt	ccagggctgc	taggaaaagg	60
aatgggcaga	cacaggtgta	tgccaatgtt	tctgaaatgg	gtataatttc	gtcctctcct	120
tcggaacact	ggctgtctct	gaagacttct	cgctcagttt	cagtgaggac	acacacaaaag	180
acgtgggtga	ccatgttggt	tgtgggggtgc	agagatggga	gggggtggggc	ccaccttgga	240
agagtggaca	gtgacacaag	gtggacactc	tctacagatc	actgaggata	agctggagcc	300
acaatgcatg	aggcacacac	acagcaagga	tgacnctgta	aacatagccc	acgctgtcct	360
gngggcactg	ggaagcctan	atnaggccgt	gagcanaaag	aaggggagga	tccactagtt	420
ctanagcggc	cgccaccgcg	gtgganctcc	ancttttgtt	cccttttagtg	agggttaatt	480
gcgcgcttgg	cntaatcatg	gtcatanctn	tttcctgtgt	gaaattgtta	tccgctcaca	540
attccacaca	acatacganc	cggaaacata	aantgtaaac	ctggggtgcc	taatgantga	600
ctaactcaca	ttaattgcgt	tgcgctcact	gcccgccttc	caatcnggaa	acctgtcttg	660
ccncttgcat	tnatgaatcn	gccaaacccc	ggggaaaagc	gtttgcgttc	tgggcgctct	720
tccgcttccct	cnctcantta	ntccctncnc	tccgtcattc	cggctgcngc	aaaccgggtc	780
accnccctcca	aaggggggtat	tccggtttcc	ccnaatcggg	gganance		828

<210> 5
 <211> 834
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(834)
 <223> n = A,T,C or G

<400> 5

tttttttttt	tttttactga	tagatggaat	ttattaagct	tttcacatgt	gatagcacat	60
agttttaatt	gcatecaaaag	tactaacaaa	aactctagca	atcaagaatg	gcagcatgtt	120
atttttataac	aatcaacacc	tgtggctttt	aaaatttggt	tttcataaga	taattttatac	180
tgaagtaaat	ctagccatgc	ttttaaaaaa	tgcttttaggt	cactccaagc	ttggcagtta	240
acatttgcca	taaacaataa	taaaacaatc	acaatttaat	aaataacaaa	tacaacattg	300
taggccataa	tcatatacag	tataaggaaa	aggtggtagt	gttgagtaag	cagttattag	360
aatagaatac	cttggcctct	atgcaaatat	gtctagacac	tttgattcac	tcagccctga	420
cattcagttt	tcaaagtagg	agacagggtc	tacagtatca	ttttacagtt	tccaacacat	480
tgaaaacaag	tagaaaatga	tgagttgatt	tttattaatg	cattacatcc	tcaagagtta	540
tcaccaaccc	ctcagttata	aaaaattttc	aagttatatt	agtcataata	cttgggtgtgc	600
ttatttttaa	ttagtgtctaa	atggattaag	tgaagacaac	aatgggtccc	taatgtgatt	660
gatattggtc	atttttacca	gcttctaaat	ctnaactttc	aggcttttga	actggaacat	720
tgnatnacag	tgttccanag	ttncaaccta	ctggaacatt	acagtgtgct	tgattcaaaa	780

tggtattttg ttaaaaatta aattttaacc tgggtggaaaa ataatttgaa atna

834

<210> 6
<211> 818
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(818)
<223> n = A,T,C or G

<400> 6

tttttttttt	tttttttttt	aagaccctca	tcaatagatg	gagacataca	gaaatagtca	60
aaccacatct	acaaaatgcc	agtatcaggc	ggcggtctcg	aagccaaagt	gatgtttgga	120
tgtaaaagtga	aatattagtt	ggcggatgaa	gcagatagtg	aggaaagttg	agccaataat	180
gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatgtt	gagccgtaga	tgccgtcgga	240
aatggtgaag	ggagactcga	agtactctga	ggcttgragg	agggtaaaat	agagaccag	300
taaaattgta	ataagcagtg	cttgaattat	ttggtttcgg	ttgttttcta	ttagactatg	360
gtgagctcag	gtgattgata	ctcctgatgc	gagtaatacg	gatgtgttta	ggagcgggac	420
ttctagggga	tttagcgggg	tgatgcctgt	tgggggccag	tgccctccta	gttggggggt	480
aggggctagg	ctggagtggt	aaaaggctca	gaaaaatcct	gcgaagaaaa	aaacttctga	540
ggtaataaat	aggattatcc	cgtatcgaag	gcctttttgg	acaggtcggg	tgtggtggcc	600
ttggtatgtg	ctttctcgtg	ttacatcgcg	ccatcattgg	tatatgggta	gtgtgttcgg	660
ttantanggc	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	ngggtctggg	ctnggtttta	cccnaccat	780
ggaatncnc	ccccggacna	ntgnatccct	attcttaa			818

<210> 7
<211> 817
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G

<400> 7

tttttttttt	tttttttttt	tggctctaga	gggggtagag	ggggtgctat	agggtaaata	60
cgggccctat	ttcaaagatt	tttaggggaa	ttaattctag	gacgatgggt	atgaaactgt	120
ggtttgctcc	acagatttca	gagcattgac	cgtagtatac	ccccggtcgt	gtagcgggtga	180
aagtggtttg	gttttagacgt	ccgggaattg	catctgtttt	taagcctaata	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatggggggt	tcaatcggga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcaggtcgcc	tggttctagg	aataatgggg	360
gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggg	gttctcctag	gttcaatacc	420
attggtggcc	aattgatttg	atggtaaggg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
aggatnccct	ngggatggga	aggcnatnaa	ggactangga	tnaatggcgg	gcangatatt	540
tcaaacngtc	tctanttctt	gaaacgtctg	aaatgttaat	aanaattaa	tttngttatt	600
gaatnttnng	gaaaagggct	tacaggacta	gaaaccaa	angaaaanta	atnntaangg	660
cnttatcntn	aaaggtmata	accnctccta	tnatcccacc	caatngnatt	ccccacnenn	720

```
acnattggat nccccanttc canaaanggc ccccccccg tgnannccnc cttttgttcc 780
cttnantgan gggtatttenc ccttngcntt atcancc 817
```

```
<210> 8
<211> 799
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G
```

```
<400> 8
catttcggg tttactttct aaggaaagcc gagcggagc tgctaacgtg ggaatcgggtg 60
cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt 120
ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag 180
tacgaacagc gctgaaagt gctggagcgg gaggtccagc agtgtagccg cgtcctgggg 240
tgggtggcgg angcctganc cgctctgctt tgtgcccc angtgggccc ccacccctg 300
acctgcctgg gtccaaacac tgagccctgc tggcggactt caagganaac cccacangg 360
ggattttgct cctanantaa ggctcatctg ggctcggcc ccccacctg gttggccttg 420
tctttgangt gagccccatg tccatctggg cactgtcng gaccacctt ngggagtgtt 480
ctccttacia ccacannatg cccgctcct cccggaaaacc antccancc tnggaaggat 540
caagnccctgn atccactnnt nctanaaccg gccnccnccg cngtggaaacc cnccttntgt 600
tccttttctt tnagggttaa tnnccgcttg gccttnccan ngctcctncc ntcttcnnc 660
gttnaaattg ttangenccc nccntcccn cncnncnan cccgaccnn annntnnann 720
nccgggggt nccnncgat tgaccnnc nccctntant tgccttnggg ncnntgccc 780
cttccctct nggganncg 799
```

```
<210> 9
<211> 801
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G
```

```
<400> 9
acgccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtgggttg 60
taangatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct 120
caaggacaag gccaccaggt gcgggggccc aagcccacat gatccttact ctatgagcaa 180
aatccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang 240
caggtcattg ggttgtnnc caactggggg ccncaacgca aaanggcna gggcctcngn 300
caccatccc angacgcggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360
ttentacccg cgnatntgtc ccantgttt cngtgcenac tccancttct nggacgtgcg 420
ctacatacgc cgggantcnc nctccgctt tgtccctatc cactnccan caacaaattt 480
cncctantg caccnattcc cacttttnc agntttccnc nncngcttc cttntaaaag 540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn cccctnata 600
gctgaantcc ccatnaccnn gntcnatgg anccntcent tttaannacn ttctnaactt 660
```

```

gggaanance ctcgnccntn cccccnttaa tccnccttg cnangnnent ccccnntcc 720
nccnnntng gcntntnann cnaaaaaggc cennnancaa tctcctnnen cctcantcg 780
ccanccctcg aaatcgccn c 801

```

```

<210> 10
<211> 789
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 10
cagctctatnt ggccagtgtg gcagctttcc ctgtggctgc cgggtgccaca tgcctgtccc 60
acagtgtggc cgtgggtgaca gcttcagccg cctcaccgg gtccaccttc ccagccctgc 120
agatccctgcc ctacacactg gcctccctct accaccggga gaagcaggtg ttcctgcccc 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttccctgc 240
caggccctaa gcctggagct ccttcccta atggacacgt ggggtgctgga gccagtgccc 300
tgctcccacc tccaccggcg ctctggggg cctctgccc tgatgtctcc gtacgtgtgg 360
tggtgggtga gccaccgan gccaggggtg ttccggccg gggcatctgc ctggacctcg 420
ccatectgga tagtgcttcc tgctgtccca ngtggccca tccctgttta tgggtcccat 480
tgtccagctc agccagctct tcaactgcta tatggtgtct gccgcaggcc tgggtctggt 540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa ataactcagcg 600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgct cactgggtcc aactccccgc 660
tccgtttaac cccatggggc tgccggcttg gccgccaat tctgttgctg ccaaanatnat 720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncant nggggggtng 780
gngtctccc 789

```

```

<210> 11
<211> 772
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(772)
<223> n = A,T,C or G

```

```

<400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60
tttgttaaat aaataagtta aatattttaa tgctgtgtc tctgtgatgg caacagaagg 120
accaacaggc cacatcctga taaaaggtaa gagggggggt gatcagcaaa aagacagtgc 180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata 240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300
ctacattaaa cgaagctgca ggttaagggg ctlanagatg ggaaaccagg tgactgagtt 360
tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa ccttctggc 480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana 540
aactggggaa aaaagaaaag gacgcccann ccccagctg tgcanctacg cacctcaaca 600

```



```

gcacaggggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact nggggggggca 660
accccggcac ccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720
ggcccnccac ccnaatntt gctgggaaat ttttctccc ctaaattntt tc 772

```

```

<210> 12
<211> 751
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

```

```

<400> 12
gcccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tctgagcct tttgcttggg gcaggtttca 120
ttggctgtgt tggtagcgt gtcattgcaa cagaatggg gaaaggcact gttctctttg 180
aagtanggtg agtctcctc atccgtatag ttgggtgaagc cacagcactt gagecccttc 240
atgggtgggtg tccacacttg agtgaagtct tcttgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360
agcagctgcn acctcagcaa tgagatgan gaggangatg aagaagaacg tcnegagggc 420
acacttgctc tcagtcttan caccatanca gccntgaaa accaananca aagaccacna 480
cnccggctgc gatgaagaaa tnaccccneg ttgacaaact tgcattggcac tggganccac 540
agtggcccn aaaaatcttc aaaaggatgc cccatcnatt gaccccccaa atgcccactg 600
ccaacagggg ctgccccacn cnennaacga tgancnatt gnacaagatc tncntgggtc 660
tnatnaacnt gaacctgcn tngtggctcc tggtcaggnc cninggcctga cttctnaann 720
aangaactcn gaagncacca gngganannc g 751

```

```

<210> 13
<211> 729
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(729)
<223> n = A,T,C or G

```

```

<400> 13
gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgtcctt 60
tgtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc 120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180
ctgtgtgggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcacccctt 240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300
ctcatcgagc ccggcgcttg ggtcttagct ctagggtttc tgggctgcta tgggtgctaag 360
actgagagca agtgtgccc cgtgacgttc ttcttcatcc tctctctcat cttcattgct 420
gaggttgcaa tgetgtggtc gccttgggtg acaccacaat ggctgagcac ttctgacgt 480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcaactcaag 540
gttggaaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600
gaagantcac ctacttcaaa gaaaanagt cttttccccc atttctgttg caattgacaa 660

```

acgtccccaa cacagccaat tgaaaacctg cacccaaccc aaanggggtcc ccaaccanaa 720
 attnaagg 729

<210> 14
 <211> 816
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(816)
 <223> n = A,T,C or G

<400> 14
 tgctcttctt caaagttgtt cttgttgcca taacaaccac cataggtaaa gcggggcgag 60
 tggtcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tctgtgtct 120
 ggcaggcca cgcagtgcct tttgtcactg gggaaatgga tgcgctggag ctctgcaaag 180
 ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggggtgtct 240
 tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaaactg ggtgggctga 300
 cangtgccag agcacactgg atggcgccct tccatgnnan gggccctgng ggaaagtccc 360
 tganccecan anctgcctct caaangcccc accttgacac ccccgacagg ctagaatgga 420
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaance ancccntaa acaaactctt 480
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaacccca gccngcgaac 540
 caancttggt tggatnccaa gcnataatct nctnttctgc ttggtggaca gcaccanrna 600
 ctgtnnanct ttagncctng gtcctcttgg gttgnncttg aacctaatcn ccnntcaact 660
 gggacaaggt aantngcctt ccttttaatt cccnancntn cccctggtt tgggggtttt 720
 cncnctccta cccagaaan nccgtgttcc cccccaacta ggggcnaaa ccnnttnttc 780
 cacaacctn cccacccac gggttcngnt ggttng 816

<210> 15
 <211> 783
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(783)
 <223> n = A,T,C or G

<400> 15
 ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg 60
 atgtggaaaa cacagattgg cgctactgc ggggtgacac ggatgtcagg gtagagagga 120
 aagacccaaa ccagggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga 180
 cagtgactag ctacagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca 240
 ccaagcagac agaagactac tgctctgcct ccaacaangt gggctcgtgc cggggctctt 300
 tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttctgt tatggaggct 360
 gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggtg 420
 tgcaagggtg gcctttgana ngcanctctg gggctcangc gactttcccc cagggccctt 480
 ccatggaaag gcgccatcca ntgttctctg gcacctgtca gccacccag ttccgctgca 540
 ncaatggctg ctgcacnac antttcctng aattgtgaca acaccccca ntgccccaa 600
 ccctcccaac aaagcttccc tgttnaaaaa taenccantt ggcttttnac aaacncccg 660

```

cncctccttt ttccccnntn aacaaagggc nctngenttt gaactgcccn aaccnnggaa 720
tctnccnngg aaaaantncc ccccttggtt cctnnaance cctccncnaa anctncccc 780
ccc 783

```

```

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 16
gccccaatc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tcgtgagcct ttgcttggt gcagggtttca 120
ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
aagtaggggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtca gccattgttg tgtacaccaa ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
ccngctgcga atgaaagaaa ntacccacgt tgacaaactg catggccact ggacgacagt 540
tgccccgaan atcttcagaa aagggatgcc ccctcgattg aacacccana tgccactgc 600
cnacagggct gcncncncn gaaagaatga gccattgaag aaggatcttc ntggctctta 660
tgaactgaaa cntgcatgg tggccctgt tcagggctct tggcagtga tictganaaa 720
aaggaacngc nttagcccc ccaaangana aaacaccccc ggggtgttgc ctgaattggc 780
ggccaaggan cctgccccn g 801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgccctgcca ctgagtggca acacccggga gctgttttgt 60
cttttggtga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgttca gcttcattaa gaccatgatg atcctcttca atttgctcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300
cttctcatc gcagccggcg ttgtggtctt tgcctttggt ttccctgggct gctatggtgc 360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatcttcat 420
tgctgaagtt gcagctgctg tggctgcctt ggtgtacacc acaatggctg aaccattcct 480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc 540
aantntggaa caccnccatg aaaagggtc caatttctgn tggcttcccc aactataccg 600

```

```

gaatttttgaa agantcncnc tacttccaaa aaaaaanant tgccttttnc cccntttctgt 660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa 720
caaaaaaant nnaagggttn 740

```

```

<210> 18
<211> 802
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(802)
<223> n = A,T,C or G

```

```

<400> 18
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120
ggatacactt tacttttagca gccaggggtga caactgagag gtgtcgaagc ttattcttct 180
gagcctctgt tagtggagga agattccggg cttagctaa gtatcagcg tatgtcccat 240
aagcaaacac tgtgagcagc cggaaggtag aggcaagtc actctcagcc agctctctaa 300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360
ggatgagtgt ggccagcgct gccccttgg ccgacttggc taggagcaga aattgctcct 420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480
gctcaggatg tccagagacg tggttccgcc cctcncctta atgacaccgn ccanncaacc 540
gtcggtctcc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cncacttgc 600
aancttcgtc nggcccattg aattcaccnc accggaactn gtangatcca ctnnttctat 660
aacggngcgc caccgcnntt ggaactccac tctnttnc tttacttgag ggtaaggtc 720
acccttnncg ttaccttggg ccaaaccntn cctgtgtcg anatngtnaa tcnggncna 780
tncanccnc atangaagcc ng 802

```

```

<210> 19
<211> 731
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 19
cnaagcttcc aggtnacggg ccgnaance tgaccnagg tancanaang cagncngcgg 60
gagccaccg tcacngngng gngtctttat nggagggggc ggagccacat cncgtggacnt 120
cntgacccca actcccccnc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180
caggaaccaa gancaaannc tgcctcncnt caagtcggcn nagggggcgg ggctggccac 240
gcncatccnt cnagtgtgn aaagcccnnc cctgtctact tgtttggaga acngcnnga 300
catgccagn gttanataac nggngagag tnannttgc tctcccttcc ggctgcgcan 360
cngtntgt tagnggacat aacctgacta cttaactgaa ccnngaate tncnccct 420
ccactaagct cagaacaaaa aacttcgaca ccaactcant gtcacctgnc tgctcaagta 480
aagtgtacc catncccaat gtntgctnga ngtctgncc tgcnttangt tcggctcctgg 540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600

```

```

cnnccntcca aggggggggnc ggcccccaat ccccccaacc ntnaattnan tttancccn 660
ccccnggcc cggcctttta cnancntcnn nnaengggna aaaccnnngc tttncccaac 720
nnaatccncc t 731

```

```

<210> 20
<211> 754
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(754)
<223> n = A,T,C or G

```

```

<400> 20
tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
caacccccc c ntccaaatnn ccttttccgg gnggggggtc caaacccaan ttanntttgg 120
annttaaat aaatnttntt tggnggggna anccnaatgt nangaaagt naaccanta 180
tnacttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
aaatngttna nggaaaaccc aanttctcnt aagggtgtt gaaggntnaa tnaaaanccc 300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa 360
ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg 420
gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggncccc cccntccgg 480
ggttngggnc aggnccnaat tgtttaaggg tccgaaaaat cctccnaga aaaaaanctc 540
ccaggntgag nntnggggtt ncccccccc canggccct ctcgnanagt tgggggttgg 600
ggggcctggg attttnttt cctntttnc tcccccccc ccnggganag aggttngngt 660
tttntcnnc ggcccnccn aagantttt ccganttnan ttaaatecnt gcctnggcga 720
agtcnttgn agggntaaan ggccccctnn cggg 754

```

```

<210> 21
<211> 755
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(755)
<223> n = A,T,C or G

```

```

<400> 21
atcancccat gaccccaac nngggaccnc tcancgggnc nnnccnaccnc cgcccnatca 60
nngtnagnnc actncnnttn natcaacccc cncnactac gcccnananc cnacgcnccta 120
nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240
nnccnccan at gattttcctn anccgattac centncccc tancctctcc cccccacna 300
cgaaggcnct ggncnaagg nngcgnccnc ccgctagntc cccnnaagt cncncccta 360
aactcanccn nattacncc ttentgagta tcaactcccc aatctcacc tactcaactc 420
aaaaanactn gatacaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480
ttagngttcc ntnaancntc ctaatacttc cagtctncc tcnccaattt ccnaangget 540
ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgcc ttctnngaac 600
gggctcntct tttccttcgg ttancctggn ttcnccggc cagttattat ttccntttt 660

```

```

aaattcctnc cntttanttt tggccttcna aacccccggc cttgaaaacg gccccctggt 720
aaaaggttgt tttganaaaa tttttgtttt gttcc 755

```

```

<210> 22
<211> 849
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(849)
<223> n = A,T,C or G

```

```

<400> 22
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt 60
acgctnggan taangcgacc cgantttctag gannncctt aaaatcanac tgtgaagatn 120
atcctgnnaa cggaanggtc accggnggat nntgctaggg tgnccnctcc cannncttn 180
cataactcng nggcccctgc caccaccttc ggcggcccng ngcccggccc cgggtcattn 240
gnnttaaccn caatnngcna ncggtttccn nccccnncng acccnggcga tccgggggtnc 300
tctgtcttcc cctgnagncn anaaantggg ccncggncct ctttaccctt nnacaagcca 360
cngcctteta ncncngccc cccctccant nnggggggact gccnanngt ccgtttctng 420
nnaccccnnn gggtnccctg gttgtcgant cnaccgnang ccanggatc cnaaggaagg 480
tgcgttnttg gcccctaccc ttgcgtncgg nncacccttc ccgacnanga nccgctcccg 540
cncnncgng cctncctcg caacaccgc nctctcngt ncggnnncct ccccaccgc 600
nccctcncnc ngncgnancn ctccnccnc gtctcannca ccaccccgcc ccgcacggcc 660
ntcanccacn ggnngacnng nagnccnntc gcnccgcgcn gcgnncctt cgcncngaa 720
ctnctcngg ccantnccg tcaanccna cnaaacgccg ctgcgcggcc cgnagcgncc 780
ncctcncga gtctcccgcn ctccnacc cangnttcn cgaggacacn nnaccccgcc 840
nncangcgg 849

```

```

<210> 23
<211> 872
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(872)
<223> n = A,T,C or G

```

```

<400> 23
gcgcaaaacta tacttcgctc gnactcgtgc gcctcgtcnc tcttttcctc cgcaaccatg 60
totgacnanc ccgattnggc ngatatchan aagntcganc agtccaaact gantaacaca 120
cacacnncn aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc 180
nggggaatcg taatnaggcg tgcgcgcgca atntgtcnc gtttatntn ccagctcnc 240
ctnccnacc tacttcttcn nagctgtcnn acccctngtn cgnaccccc naggtcggga 300
tcgggtttnn nntgaccgng cnnccctcc cccctccat nacganccnc ccgcaccacc 360
nanngcncgc nccccgnct cttegcnc cgtctctn cccctgtngc ctggcncngn 420
accgcattga cctcgcncn ctncnngaaa ncgnanacgt ccgggttggn annancgctg 480
tgggnnngcg totgcncgc gttccttcn ncncttcca ccattctct tacnggggtc 540
ccncgcctc tcnncacnc cctgggacgc tntcctntgc ccccttnac tccccctt 600

```

```

cgncgtgncc cgnccccacc ntcatttnca nacgntcttc acaannncc ggntnnctcc 660
cnancngnncn gtcancnag ggaagggngg ggnncnntg nttgacgttg ngngngangtc 720
cgaanantcc tcncntcan cncctaccct cgggcggnct ctengttnc aacttancaa 780
ntctcccccg ngngcnctc tcagcctcnc cnccccncct ctctgcantg tncctcgtc 840
tnaccnntac gantnttcgn cncctcttt cc 872

```

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

```

gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggctnta 60
nctgncttcc tgtgtcaaat gtatacnaa tanatatgaa tctnatntga caaganngta 120
tcntncatta gtaacaantg tnntgtccat cctgtcngan canattccca tnnattncgn 180
cgcattcnnc gncantatn taatngggaa ntcnnntnn ncaccnncat ctatcntncc 240
gcncctgac tggagagat ggainanttc tnntntgacc nacatgttca tcttgattn 300
aanancccc cgngnccac cgggtngng cngccnntc ccaagacctc ctgtggaggt 360
aacctgcgtc aganncatca aacntgggaa acccgcncc angtnnaagt ngnnncanan 420
gateccgtcc aggttnnacc atcccttenc agegccccct ttngtgcctt anagnnagc 480
gtgtccnanc cnccaacat ganacgcgcc agnccanccg caattnggca caatgtcgn 540
gaacccccca gggggantna tncaaanccc caggattgtc cncncangaa atcccnanc 600
ccnccctac cncctttgg gacngtgacc aantcccgga gtnccagtcc ggcngnctc 660
ccccaccgtt nncntgggg ggggtgaant cngnntcanc cngncgaggn ntagnaagga 720
accggnccn ggncgaanng ancnntcnga agnccnnt cgtataacct cccctcncca 780
nccnacngnt agntcccccc cngggtnccg aangg 815

```

<210> 25

<211> 775

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(775)

<223> n = A,T,C or G

<400> 25

```

ccgagatgtc tcgtccgtg gccttagctg tgcctcgct actctctctt tctggcctgg 60
aggctatcca gcgtactcca aagattcagg ttactcacg tcatccagca gagaatggaa 120
agtcaaatct cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttact 180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg 240
actggtcttt ctatctctng tactacactg aattcacccc cactgaaaaa gatgagtatg 300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca 360
tgtaagcagn cncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt 420
ctgcttgctt gcnttttaat antgatatgc ntatacacc taccctttat gnccccaaat 480

```

```

tgtaggggtt acatnantgt tcnctnngga catgatcttc ctttataant cncncnttcg 540
aattgcccgt cncncngttt ngaatgtttc cnaaaccacg gttgggtccc ccaggtcncc 600
tcttacggaa gggcctgggc cnccttncaa ggttggggga accnaaaatt tcncttntgc 660
cncncncca cnccttngng nncncanttt ggaacccttc cnattcccct tggcctcnaa 720
nccttnncta anaaaacttn aaancgtngc naaanntttt acttcccccc ttacc 775

```

<210> 26

<211> 820

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(820)

<223> n = A,T,C or G

<400> 26

```

anattantac agtghtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat 60
cccanagata ncttatanca acagtgtttt gaccaagagc tgctgggcac atttcttgc 120
gaaaagggtg cgggtcccat cactcctcct ctcccatagc catcccagag ggggtgagtag 180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca 240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg ggggtggcna nganagccta 300
netgaggggt cacactataa acgttaacga ccnagatnan cacctgttc aagtgcaccc 360
ttctacctg acnaccagn accnnnaact gcngcctggg gacagcctg ggancageta 420
acnnagcact cacctgcccc cccatggccg tncgntccc tgggtcctgnc aagggaaget 480
ccctgttga attncggga naccaaggga nccccctct ccanctgtga aggaaaaann 540
gatggaattt tnccttccg gccnntccc tcttcttta cagccccct nntactctc 600
tccctctntt tncctgnnc acttttnacc ccnnnatttc ccttnattga tggannctn 660
ganattccac tncgctcnc cntcnatng naanacnaaa nactntctna ccnggggat 720
gggnnccctg ntcactctt ctttttctt accnccnntt ctttgctct ccttngatca
780tccaacntc gntggcctn cccccnnn tcttttccc 820

```

<210> 27

<211> 818

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(818)

<223> n = A,T,C or G

<400> 27

```

tctgggtgat ggctcttcc tctcagga cctctgactg ctctgggcca aagaatctct 60
tgtttcttct ccgagcccca ggcagcgggtg attcagcctt gcccaacctg attctgatga 120
ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggagc 180
ctgctgagca cttccgcccc tcacctgcc cagccctgc catgagctct gggctgggtc 240
tccgcctcca gggttctgct cttccangca nccancaaag tggcgtggg ccacactggc 300
ttcttctgc ccntccctg gctctgante tctgtcttcc tgtcctgtgc angcncctg 360
gatctcagtt tccctcctc anngaactct gtttctgann tcttcantta actntgantt 420
tatnaccnan tggnetgtnc tgtcnnactt taatgggcn gaccggctaa tccctccctc 480

```



```

nctcccttcc atttcnnnna accngettnc cntcntctcc ccntancccg ccngggaanc      540
ctccttttgc ctnaccangg gccnnnaccg ccctnnctn ggggggcng gttnctncnc      600
ctgntnnccc cnetcncrnt tncctegtec cnnncncgcn nngcannttc ncngtcccn      660
tnnctctttn ngntnecnaa ngntcncntn tnnnnngnch ngntnntnch tccctctenc      720
cnnntgnang tnnntnnnnc ncngnnccccc nnnnnnnnnn nggnntnnn tctnncngc      780
cccnccccc ngnattaagg cctccntct cgggcnc      818

```

```

<210> 28
<211> 731
<212> DNA
<213> Hcno sapien

```

```

<220>
<221> misc_feature
<222> (1)...(731)
<223> n = A,T,C or G

```

```

<400> 28
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg      60
tcccaacatg anggtgnggt tctcttttga angaggggtg ngtttttann ccnggtgggt      120
gattnaaccc cattgtatgg agnnaaaagg tttnagggat ttttcggctc ttatcagtat      180
ntanattcct gtnaatcgga aaatnatntt tcnnccggaa aatnttgctc ccatccgnaa      240
attnctcccg ggtagtgcac nttngggggg cngccangtt tcccaggctg ctanaatcgt      300
actaaagntt naagtgggan tncaaatgaa aacctnnac agagnatccn taccggactg      360
tnnnttncct tcgcccctng actctgcng agcccaatac ccngngnat gtcncccn      420
nnngcgnnc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn      480
cgtttcncat naaggcactt tngcctcatc caacnctng cctcnncca tttngccgtc      540
nggttcnct acgctnntng cncctnnntn ganattttnc ccgctnggg naancctcct      600
gnaatgggta gggncctntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt      660
tctnaccccc ccccttttt caatcccanc ggcnaatggg gtctcccnng cgangggggg      720
nncccannc c

```

```

<210> 29
<211> 822
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(822)
<223> n = A,T,C or G

```

```

<400> 29
actagtcag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat      60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncrnt      120
atntntacnc tcatanncct cnnnaccac tccctcttaa ccctactgt gcctatngcn      180
tnnctantct ntgcgcctn cnanccacn gtgggcnac cncnngnat ctenatctcc      240
tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaanch      300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc      360
tactctgact cccacngcct annnattagc anctcccc nacnatntct caaccaaate      420
ntcaacaacc tatctantgt ttncccaacc nttncctccg atccccnnac aacccccctc      480

```

```

ccaaataccc nccacctgac ncctaaccen caccatcccg gcaagccnan ggnccatttan 540
ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600
aatnctectn naatttactn ncantnccat caanccacn tgaaacnnaa cccctgtttt 660
tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccnctnc 720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancaggcna anannntccg 780
canatccat cccttanttn ggggnccctt nccngggcc cc 822

```

```

<210> 30
<211> 787
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(787)
<223> n = A,T,C or G

```

```

<400> 30
cgccgcctg ctctggcaca tgctctctga atggcatcaa aagtgatgga ctgcccattg 60
ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120
gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctctc atctacatna 180
gctggaagcc ctggagggcc tctctcgcca gcctcccctt tctctccacg ctctccangg 240
acaccagggg ctccaggcag cccattatcc ccagnangac atgggtgtttc tccaagcgga 300
cccatggggc ctgnaaggcc agggcctcct ttgacaccat ctctcccgtc ctgcctggca 360
ggcgtggga tocactant ctanaacggn cgcacccncc gtgggagctc cagcttttgt 420
tccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tnttctctgt 480
gtgaaattgt ttntccctc ncnattccnc ncnacatacn aacccggaan cataaagtgt 540
taaagcctgg gggtngcctn nngaattnaac tnaactcaat taattgcgtt ggctcatggc 600
ccgctttccn ttcnnggaaaa ctgctntccc ctgcnttnnt gaatcggcca cccccnggg 660
aaaagcggtt tgcnttttng ggggntccct ccncttcccc cctcnctaan cctnccgct 720
cggtcgttnc nggtngcggg gaangggnat nnnctccnc naagggggng agnnngntat 780
cccaaaa 787

```

```

<210> 31
<211> 799
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

```

```

<400> 31
tttttttttt tttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac 60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc 120
aacaaaggac tctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct 180
cccgagggtt gggggccacc agtccagggt tgggagcact acanggggtg ggagtgggtg 240
gtggctggtn cnaatggcct gncacanatc cctacgatcc ttgacacctg gatttcacca 300
ggggaccttc tgttctccca nggnaacttc nttnnatctn aaagaacaca actgtttctt 360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttgggtaca 420

```

tatgggttcg	gcccacctct	ccntcnaa	aagtaattca	ccccccccc	ccntctnttg	480
cctgggccc	taantacca	caccggaact	canttanta	ttcatcttng	gntgggcttg	540
ntnatncn	cctgaangcg	ccaagttgaa	aggccacgcc	gtncnctc	cccatagnan	600
nttttnt	canctaagc	cccccnngc	aacnatccaa	ttccccccc	tgggggcccc	660
agcccanggc	ccccgntcg	ggnnnccngn	cncgnantcc	ccaggntctc	ccantcngnc	720
ccnnngcnc	cccgacgca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtnnncac	780
ctcgcccccc	ccnncgng					799

<210> 32

<211> 789

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(789)

<223> n = A,T,C or G

<400> 32

ttttttttt	ttttttttt	ttttttttt	ttttttttt	ttttttttt	ttttttttt	60
ttttncnag	ggcaggttta	ttgacaacct	cncgggacac	aancaggctg	gggacaggac	120
ggcaacaggc	tccggcggcg	gcggcggcgg	ccctacctgc	ggtaccaa	ntgcagcctc	180
cgtcccoget	tgatnttct	ctgcagctgc	aggatgccnt	aaaacagggc	ctcgcccntn	240
ggtgggcacc	ctgggatttn	aatttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtggtnnta	ccnccnccg	ttggcncaet	ccccntggaa	accacttntc	360
gcggtcccg	catctggtct	taaaccttgc	aaacnctggg	gccctctttt	tggttantnt	420
ncnngccaca	atcatnactc	agaactggcnc	gygctggccc	caaaaaan	ccccaaaacc	480
ggnccatgtc	ttnnccgggt	tgctgcnatn	tncatcacct	cccgggcnca	ncaggncaac	540
ccaaaagtgc	ttgnggccc	caaaaaanct	ccggggggnc	ccagtttcaa	caaagtcatc	600
ccccttgggc	cccaaactct	ccccccgntt	netgggtttg	ggaacccacg	cctctnnctt	660
tggnnggcaa	gntggntccc	ccttcggggc	ccgggtgggc	ccnctcttaa	ngaaaaacnc	720
ntcctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tcctttttt	tanaaacggg	780
ccccccncg						789

<210> 33

<211> 793

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(793)

<223> n = A,T,C or G

<400> 33

gacagaacat	gttggatggt	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
aattcatggc	tgttgagca	atanaacccc	agttctacga	gctgctgac	aaaggacttg	120
gactaaagtc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtttgc	agatgtattt	gcaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggttggtcat	catgatcaca	300
acaangaacg	gggctcggtt	atcaccantg	aggagcagga	cgtgagcccc	cgcctgcac	360

```

ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct 480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccacc cccggggaaa aggcngtttg cttnttgggg 720
cgcncctccc gctttctcgc ttcttgaant ccttcccccc ggtctttcgg cttgcggcna 780
acggtatcna cct 793

```

```

<210> 34
<211> 756
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(756)
<223> n = A,T,C or G

```

```

<400> 34
gcgcgcaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag cccaatctt 60
ancaagtgcg gggaanagct gggctgactc aagctagtct ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgatga catactggag 180
atcggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttctct ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtgcg tgcceaanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcttgg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcng ggttgctcca gaaaggetnc aanaanatcc ttttcnctga aggcctcccg 600
atncnctagt nctagaatcg gccgcacatc gcggtgganc ctccaacctt tcgttnccct 660
ttactgaggg ttntattgccg cccttggcgt tatcatggct acnccngttt cctgtgttga 720
aattnttaac ccccacaaat tccacgcna cattng 756

```

```

<210> 35
<211> 834
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(834)
<223> n = A,T,C or G

```

```

<400> 35
gggatctct anactnacct gnatgcatgg ttgtcgggtg ggtcgtctgc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggtc gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cncctcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct cggatgaactc gatgacnang ggcagctggg tgtgtntgat 240
aaantccanc angttctcct tggtagctc ccttcaaaag ttgttcgggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt 360

```

```

ggaaactgat cccaaatggg atgtcatcca tgcctctgc tgcctgcaaa aaacttgctt 420
ggcncaaadc cgactcccn tccctgaaag aagccnatca cccccccctc cctggactcc 480
nncaangact ctncgcgtnc cccntccnng caggggttgg ggcanncgg gccentgcgc 540
ttcttcagcc agttcacnat ntcatcagc cctctgccca gctgttntat tccctggggg 600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcncnt 660
acntnctggg ccgggttcaa antccctccn ttgcnntcn cctcgggcca ttctggattt 720
nccnaacttt ttccttcccc cccccnccg ngtttggntt tttcatnggg ccccaactct 780
gctnttggcc antcccttgg gggcntntan cccccctnt ggtcccntng ggcc 834

```

```

<210> 36
<211> 814
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(814)
<223> n = A,T,C or G

```

```

<400> 36
cggnccgttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn 60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcca 120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tgggtctctcc accccctgta 180
ggaaaggcct gcttgtaag acaccacaat ncggctgaat ctnaagtctt gcgttttact 240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca 300
ctaaaacanc ccagcgtca cttctgcttg ganaaatatt ctttgcctt ttggacatca 360
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
aggggangtc ntttncagt gatctgcca anantaccn tatcatcnnt gaataaaaag 540
gcccctgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatggtgcc 600
cttccggtct gatccnaaag gaatgttctt gggctccant cctcctttg ttnttacgt 660
tgtnttgac cnttgctngn atnaccaan tganatcccc ngaagcacc tnccttggc 720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcnccnaan 780
ggngaactca agaaggctcn ngaaaaacca cncn 814

```

```

<210> 37
<211> 760
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(760)
<223> n = A,T,C or G

```

```

<400> 37
gcatgtgct ctctctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60
gcgcagtgtt cgctgaagg gttgtagtac cagcgcggga tgctctcct gcagagtct 120
gtgtctggca ggtccacgca atgcccttg tctctgggga aatggatgcg ctggagctcg 180
tcnaanccac tctgtatatt ttacangca gcctcctccg aagctccgg gcagtgggg 240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgtgcagc ggaactgggt 300

```

```

gggctgacag gtgccagaac acactggatn ggcccttcca tggaagggcc tgggggaaat 360
cncctnancc caaactgcct ctcaaaggcc accttgcaca ccccgacagg ctagaaatgc 420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aacccaaanc 480
ttgcaaaatc tgctccgtgg gggtcattnn taccanggtt ggggaaanaa acccggcngn 540
gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca 600
caattgaact gttaacnttg ggccnggttc cctnnggtg gtctgaaact aatcacgcgc 660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtntttt 720
ctctctncc ctaaaaatcg tnttcccccc cntanggcg 760

```

<210> 38

<211> 724

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(724)

<223> n = A,T,C or G

<400> 38

```

tttttttttt tttttttttt tttttttttt tttttaaaaa cccctcccat tgaatgaaaa 60
cttcnnaaat tgtccaaccc cctcncccaa atnccattt cggggggggg gttccaaacc 120
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180
aatttaaccc attatnaact taaatnccn gaaaccctg gnttccaaaa atttttaacc 240
cttaaatccc tccgaaattg ntaanggaaa accaaatcn cctaaggctn tttgaagggt 300
ngatttaaac ccccttnant tnttttnacc cnnngctnaa ntatttngnt tccggtgttt 360
tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt 420
tttttgaatt ggaaattccn ngggaattna ccgggggttt tcccttttgg gggccatncc 480
ccncttttgc gggtttgggn ntagggtgaa tttttnnang nccccaaaaa ncccccaana 540
aaaaaactcc caagnnttaa ttngaatttc ccccttccca ggcccttttgg gaaaggnggg 600
ttnttggggg ccngggantt cnttcccccn ttncnccccc cccccnggt aaanggttat 660
ngnntttggt ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggnccg 720
gccg 724

```

<210> 39

<211> 751

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(751)

<223> n = A,T,C or G

<400> 39

```

tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60
caacacaata tttatttcat ttgtttcttt tatttccattt tatttgtttg ctgctgctgt 120
tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180
ggccgcctta agctttctaa atttgaaca tctaagcaag ctgaanggaa aagggggttt 240
cgcaaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttaattana 360

```

```

cttggggggtt ccctccccc anccaaccccn ctgacaaaaa gtgcengccc tcaaatnatg 420
tcccggcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccnncnc caggtnaaaa 480
tgaagggtta ccatntttta cncacactcc acntggcnnn gcctgaatcc tcnaaaancn 540
ccctcaancn aattnctnng ccccggtcnc gcntnngtcc cncccggggt cggggaantn 600
cacccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660
cnnagactnt cctcnncnan cncaattttc tttntntcac gaacncgnnc cnnaaaatgn 720
nnnnncctc cncngtcen naatcnccan c 751

```

<210> 40

<211> 753

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(753)

<223> n = A,T,C or G

<400> 40

```

gtggtatttt ctgtaagatc aggtgttcct cctcgtagg tttagaggaa acaccctcat 60
agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg 120
cgccctatgc acagctgggc ccttgagaca gragggttc gatgtcaggc tcgatgtcaa 180
tggctctggaa gcgycggctg tacctgcgta ggggcacacc gtcagggccc accaggaact 240
tctcaaagt ccaggcaacn tcgttgcgac acaccggaga ccagggtgatn agcttggggt 300
cggtcataan cgcggtggcg tcgtcgtgag gagctggcag ggcctcccgc aggaaggcna 360
ataaaagggt cgcccccgca ccgttcant cgcacttctc naanaccatg angttggggt 420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gcctanctg gttgcccn gn atgccaanca nccccaancc cgggggtcct 540
aaanccccc cctcctcntt tcactctgggt tntntcccc ggacctgggt tcctctcaag 600
ggancccata tctcnaccan tactcacnt nccccccnt gnnaaccanc cttctanngn 660
ttcccncccg ncctctgggc cntcaaanan gcttnacna cctgggtctg ccttcccccc 720
tnccctatct gnaccccn cn tttgtctcan tnt 753

```

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

```

actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gtttcaaagt 60
agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt 180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag 240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300
ttttactttt tgattaattg tgttttatat attagggtag t 341

```

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42
 acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat 60
 gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

<210> 43
 <211> 305
 <212> DNA
 <213> Homo sapien

<400> 43
 acatctttgt tacagtctaa gatgtgttct taaatcacca ttcttctctg gtcctcacc 60
 tccaggggtggt tctcacactg taattagagc tattgaggag tctttacagc aaattaagat 120
 tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca 180
 cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240
 tggatacaga acgagagtta tcttgataa ctacagagctg agtacctgcc cgggggcccgc 300
 tcgaa 305

<210> 44
 <211> 852
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(852)
 <223> n = A,T,C or G

<400> 44
 acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtr ctttgtttct 60
 gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120
 ctctccatcc tcggggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180
 ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc 240
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300
 agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga 360
 ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc 420
 acttggcagg ggggtcttgc tcttttttca tatcaggtga ctctgcaaca ggaaggtgac 480
 tgggtggtgt catggagatc tgagcccggc agaaagtatt gctgtccaac aaatctactg 540
 tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag 600
 gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcaactactgc 660
 actggccggt ccaactcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg 720
 ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctccgcttg atgtcgaact 780
 cntggaaagg gatacaattg gcacccagct ggttggtgtc caggaggtga tggagccact 840
 cccacacctg gt 852

<210> 45
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 45
 acaacagacc cttgctcgtc aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60


```

agtctgacac catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaactctt 120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacctg ctgt 234

```

```

<210> 46
<211> 590
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(590)
<223> n = A,T,C or G

```

```

<400> 46
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgta 60
atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa 120
aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta 240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatgggat 300
caggataaan aactgaaggg canaaagaat taattttcac ttcattgtaac ncacccanat 360
ttacaatggc ttaaattgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc 420
tggctctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt 590

```

```

<210> 47
<211> 774
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(774)
<223> n = A,T,C or G

```

```

<400> 47
acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60
tgaacagaat tttcctgnac aacggggcctt caaaataatt ttcttgggga ggttcaagac 120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180
cattacagac gggactctgg gaggaaggat aaacagaaaag gggacaaaagg ctaatcccaa 240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggtctt 300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg 360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc 420
ccacactcct tgaacacaca tcccaggtt atattcctgg acatggctga acctcctatt 480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540
acggcatggg aagcctttct gacttgcttg attactccag catcttggaa caatccctga 600
ttcccactc cttagaggca agataggtg gttaagagta gggctggacc acttggagcc 660
aggctgctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt 774

```

<210> 48
 <211> 124
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(124)
 <223> n = A,T,C or G

<400> 48
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120
 tgggt 124

<210> 49
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 49
 gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt 60
 tgtggctaca ggtgggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120
 ttagggcacc catatcccaa gcantgt 147

<210> 50
 <211> 107
 <212> DNA
 <213> Homo sapien

<400> 50
 acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatataattgc 60
 atggtttgag gttaggagga gttaggcata tgttttggga gaggggt 107

<210> 51
 <211> 204
 <212> DNA
 <213> Homo sapien

<400> 51
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg 60
 cggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120
 gccttgcaag gtcagaaagg ggactcaggg ctccaccac agccctgccc cacttgcca 180
 cctccctttt gggaccagca atgt 204

<210> 52

<211> 491
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(491)
 <223> n = A,T,C or G

<400> 52
 acaaagataa catttatctt ataacaaaaa tttgatagtt tttaaaggta gtattgtgta 60
 ggggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120
 ccacagaca gggtttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180
 aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaattatt 240
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtgcc ctcagtccca 300
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360
 atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat 420
 caattttatt tggataacaa agggctctca aattatattg aaaaataaat ccaagttaat 480
 atcactcttg t 491

<210> 53
 <211> 484
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(484)
 <223> n = A,T,C or G

<400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60
 gtattaacag ttgctgaagt ttggatattt tatgcagcat tttctttttg ctttgataac 120
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctget 180
 caatcaaata tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct 240
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300
 agctttgant ttctttgtgc tgatangagg aagggtgaa ttaccttgtt gcctctccct 360
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncc 420
 tancctgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480
 cant 484

<210> 54
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 54
 actaaacctc gtgcttgtga actccataca gaaaacgggtg ccacccctga acacggctgg 60
 ccactgggta tactgctgac aaccgcaaca aaaaaaacac aaatccttgg cactggctag 120
 tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55
 <211> 91
 <212> DNA
 <213> Homo sapien

<400> 55
 acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56
 <211> 133
 <212> DNA
 <213> Homo sapien

<400> 56
 ggccgatgtg cgttgggtat atacaaatat gtcattttat gtaagggact tgagtatact 60
 tggatttttg gtatctgtgg gttgggggga cggctccagga accaataccc catggatacc 120
 aagggacaac tgt 133

<210> 57
 <211> 147
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(147)
 <223> n = A,T,C or G

<400> 57
 actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60
 gactgggagc tgagcccttc cctttgcgcc tgccctcagag gattgttgcc gacntgcana 120
 tctcantggg ctggatncat gcagggt 147

<210> 58
 <211> 198
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(198)
 <223> n = A,T,C or G

<400> 58
 acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60
 tgattacata catttactct ttaaaaaaga tgtaaatctt aatttttatg ccacttatta 120
 attaccaat gagttacctt gtaaatagaga agtcatgata gcactgaatt ttaactagtt 180
 ttgacttcta agtttggt 198

<210> 59

<211> 330
 <212> DNA
 <213> Homo sapien

<400> 59
 acaacaaatg ggttgtagg aagtcttata agcaaaactg gtgatggcta ctgaaaagat 60
 ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt 120
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180
 tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagaccag 240
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60
 <211> 175
 <212> DNA
 <213> Homo sapien

<400> 60
 accgtgggtg cttctacat tcttgacggc tcttcacca acatctggtt ctacttcggc 60
 gtctggtggt cttctctctt catctcctc cagctggtgc tgctcatcga ctttgccgac 120
 tcttgaacc agcgtggtg gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61
 <211> 154
 <212> DNA
 <213> Homo sapien

<400> 61
 accccacttt tcttctgtg agcagtcctg acttctcact gctacatgat gaggtgagt 60
 ggttggtgct cttcaacagt atctctccct ttccggatct gctgagccgg acagcagtgc 120
 tggactgcac agccccgggg ctccacattg ctgt 154

<210> 62
 <211> 30
 <212> DNA
 <213> Homo sapien

<400> 62
 cgctcgagcc ctatagtgag tcgtattaga 30

<210> 63
 <211> 89
 <212> DNA
 <213> Homo sapien

<400> 63
 acaagtcatt tcagaccct ttgtcttca aaactgacca tcttttatat ttaatgcttc 60
 ctgtatgaat aaaaatggtt atgtcaagt 89

<210> 64
 <211> 97

<212> DNA

<213> Homo sapien

<400> 64

```
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag    60
aatcagtga tccaggattg gtccttggat ctggggg    97
```

<210> 65

<211> 377

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(377)

<223> n = A,T,C or G

<400> 65

```
acaacaanaa ntcccttctt taggccactg atggaaacct ggaacccccct tttgatggca    60
gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc    120
ccaaccctgg tctaccacaca nttctggcta tgggctgtct ctgccactga acatcagggg    180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa    240
ggtgctgttt gtcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg    300
tgggggtgaa ctaccccccag gaggaatcat gcctgggcga tgcaanggtg ccaacaggag    360
gggcgggagg agcatgt    377
```

<210> 66

<211> 305

<212> DNA

<213> Homo sapien

<400> 66

```
acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttcctccg ttgttgcggtg    60
agaacccgtg tgcccccttc caccatatcc accctcgctc catctttgaa ctcaaacacg    120
aggaaactaac tgcacccctgg tccctctccc agtccccagt tcacccctcca tccctcacct    180
tctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt    240
ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac    300
tgttt    305
```

<210> 67

<211> 385

<212> DNA

<213> Homo sapien

<400> 67

```
actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga    60
ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc    120
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc    180
tgtgctgtgc tggagattca cttttgagag agttctctc tgagacctga tctttagagg    240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg    300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatat    360
```

catagtttct gtgctagtg accgt

385

<210> 68
<211> 73
<212> DNA
<213> Homo sapien

<400> 68
acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa
gttttttttaa tgg

60
73

<210> 69
<211> 536
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(536)
<223> n = A,T,C or G

<400> 69
actagtcacag tgtgggtggaa ttccattgtg ttggggggctc tcaccctcct ctcctgcagc 60
tccagctttg tgctctgcct ctgaggagac catggcccag catctgagta ccctgctgct 120
cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat 180
cccggttggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt 240
cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt 300
actaagagcc aggcacacaga ccgttggggg ggtgaattac ttcttcgacg tagagggtggg 360
ccgaaccata tgtaccaagt cccagcccaa ctgggacacc tgtgccttcc atgaacagcc 420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagtccct ggggagaaca 480
gaangtcctt gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc 536

<210> 70
<211> 477
<212> DNA
<213> Homo sapien

<400> 70
atgaccccta acaggggccc tctcagccct cctaattgacc tccggcctag ccatgtgatt 60
tcacttccac tccataacgc tcctcactact aggcctacta accaacacac taaccatata 120
ccaatgatgg cycgatgtaa cagagaaaag cacataccaa ggccaccaca caccacctgt 180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc 240
agggatTTTT ctgagccttt taccactcca gcttagcccc taccceccaa ctaggagggc 300
actggccccc aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat 360
ccgtattact cgcacagga gtatcaatca cctgagctca ccatagtcta atagaaaaca 420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt 477

<210> 71
<211> 533
<212> DNA
<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(533)
 <223> n = A,T,C or G

<400> 71
 agagctatag gtacagtgtg atctcagctt tgcaaacaca ttttctacat agatagtact 60
 aggtattaat agatatgtaa agaaaagaaat cacaccatta ataatggtaa gattgggtta 120
 tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat 180
 attattttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatttcatt 240
 taaataaaagg tttgtcatct ttaaaaatac agcaatatgt gactttttta aaaagctgtc 300
 aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca 360
 agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg 420
 cttcgttaatt ttggagtang aggttccttc ctcaattttg tattttttaa aagtacatgg 480
 taaaaaaaaa aattcacaac agtatataag gctgtaaaaat gaagaattct gcc 533

<210> 72
 <211> 511
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(511)
 <223> n = A,T,C or G

<400> 72
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcggtgta 60
 aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180
 aaacatggan agattgggtgc tgganategc cgtggctatt cctcattgtt attacanagt 240
 gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300
 cacatgagaa ctgaaatggc ccaaaccacg aaagaaagcc caactagatc ctcagaanac 360
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420
 atttctctcc attgcagcna naaaccctgt cttctaagca aacncagggtg atgatggcna 480
 aaatacaccc cctcttgaag naccnggagg a 511

<210> 73
 <211> 499
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(499)
 <223> n = A,T,C or G

<400> 73
 cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac 60
 cagtgggtggc ttccagtgtg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120
 tggccttggg ggagctgggt ccagcaccag tggcagctct ggtgctgtg gtttctccta 180

caagtgagat tttagatatt gttaatcctg ccagtccttc tcttcaagcc aggggtgcac	240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca	300
ctctgcatta aatctatctt ccatttctga aaaaaaaaaa aaaaaaaggc cggccgctcg	360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc	420
catctgttgt ttgcccctcc cccgntgcct tcttgaccc tggaaagtgc cactccact	480
gtccttttct aantaatat	499

<210> 74
 <211> 537
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(537)
 <223> n = A,T,C or G

<400> 74	
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat	60
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact	120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa	180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga	240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag	300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc	360
cagtttgctt gatataattt ttgatattaa gattcctgac ttatattttg aargggctct	420
actgaaaaan gaatgatata ttcttgaaga catcgatata catctattta cactcttgat	480
tctacaatgt agaaaatgaa ggaaatgccc caaattgcat ggtgataaaa gtcccg	537

<210> 75
 <211> 467
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(467)
 <223> n = A,T,C or G

<400> 75	
caaanacaat tggtcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc	60
tgcataattac acgtacctcc tctgtctcct caagtagtgc ggtctatctt gccatcatca	120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg	180
tggcacaagg aggccatctt tctctcatcg gttattgtcc ctagaagcgt cttctgagga	240
tctagtggg ctttctttct ggggttgggc catttcannt ctcattgtgt tactattcta	300
tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa	360
caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc	420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn	467

<210> 76
 <211> 400
 <212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(400)

<223> n = A,T,C or G

<400> 76

```
aagctgacag cattcggggcc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac      60
tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc      120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat      180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag      240
acttgtcttt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca      300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng      360
ttnagtggga tcganacatg taagcagcan catgggaggt      400
```

<210> 77

<211> 248

<212> DNA

<213> Homo sapien

<400> 77

```
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc      120
caggcaactgt tcatctcagc ttttctgtcc ctttgcctcc ggcaagcgtc tctgctgaaa      180
gttcatactc ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaaa      240
aaaaaaaaa      248
```

<210> 78

<211> 201

<212> DNA

<213> Homo sapien

<400> 78

```
actagtcacg tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca      60
tcaccacagc cccgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac      120
tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttggtt ataatgcct      180
gatttaaaaa aaaaaaaaaa a      201
```

<210> 79

<211> 552

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(552)

<223> n = A,T,C or G

<400> 79

```
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg      60
```

```
<210> 80
<211> 476
<212> DNA
<213> Homo sapien
```

<400> 80

```
<210> 81
<211> 232
<212> DNA
<213> Homo sapien
```

<400> 81

```
<210> 82
<211> 383
<212> DNA
<213> Homo sapien
```

<220>
 <221> misc_feature
 <222> (1)...(383)
 <223> n = A,T,C or G

<400> 82
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60
 agtaccagta ccaataacat gccagtgccg gtgccagcac cagtgggtggc ttcagtgctg 120
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctgggtg 180
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt 240
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83
 <211> 494
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(494)
 <223> n = A,T,C or G

<400> 83
 accgaattgg gaccgctggc ttataagcga tcatgtcttc cagtattacc tcaacgagca 60
 gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc 120
 ccacctctgt cgggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180
 acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggt ccttaaactg 240
 atgtcttttc tgccacctgt taccctctcg agactccgta accaaaactct tcggactgtg 300
 agccctgatg ccttttttgc agccatactc tttggcntcc agtctctcgt ggcgattgat 360
 tatgcttgtg tgaggcaatc atgggtggcat caccatnaa gggaacacat ttganttttt 420
 tttcncatat tttaaattac naccagaata ntgcagaata aatgaattga aaaactctta 480
 aaaaaaaaaa aaaa 494

<210> 84
 <211> 380
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(380)
 <223> n = A,T,C or G

<400> 84
 gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca 60
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag 120
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
 gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctgggtg 240
 gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctgggtcac ttgctcattg 300

ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttnccg cctcatccgg 380

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctcgc ttcataccgc 60
tnccatcgtc atactgtagg tttgccacca cctcctgcat ctggggcgcg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgtctga tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtga gtcaccagcc 300
ctatcatgcc ntigaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcttgaagt gctngccgct cctcgctcct tgggggngc gcntnccttt 480
t 481

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
acttgaaaa gcaacttnaa gcctggacac tggtaataaa attcacaata tgcaaacatt 120
taaacagtgt gtcaatctgc tcccttactt tgatcacc accgtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaagcag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)...(413)

<223> n = A,T,C or G

<400> 87

agaaaccagt	atctctnaaa	acaacctctc	ataccttggtg	gacctaat	ttgtgtgcgtg	60
ttgtgtgtgcg	cgcatattat	atagacaggc	acatcttttt	tacttttgta	aaagcttatg	120
cctcttttgg	atctatatct	gtgaaagttt	taatgatctg	ccataatgtc	ttggggacct	180
ttgtcttctg	tgtaaaggt	actagagaaa	acacctatnt	tatgagtcaa	tctagttngt	240
tttattcgac	atgaaggaaa	tttccagatn	acaacactna	caaactctcc	cttgactagg	300
ggggacaaaag	aaaagcnaaa	ctgaacatna	gaaacaattn	cctgggtgaga	aattncataa	360
acagaaattg	ggtngtatat	tgaaanann	catcattnaa	acgttttttt	ttt	413

<210> 89

<211> 448

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(448)

<223> n = A,T,C or G

<400> 88

cgcagcgggt	cctctctatc	tagctccagc	ctctcgcctg	ccccactccc	cgcgccccgc	60
gtcctagccn	accatggccg	ggccccctgcg	cgccccgctg	ctcctgctgg	ccatcctggc	120
cgtggccccg	gcccgtgagcc	ccgcggcccg	ctccagctcc	ggcaagccgc	cgcgccctgt	180
gggaggccca	tggacccccg	gtggaagaag	aagggtgtgcg	gcgtgcactg	gactttgcgc	240
tcggcnanta	caacaaaccc	gcaacnactt	ttaccnagcn	cgcgctgcag	gttgtgccgc	300
cccaancaaa	ttgttactng	gggtaantaa	ttcttggaag	ttgaacctgg	gccaaacnng	360
tttaccagaa	ccnagccaat	tngaacaatt	ccccctccat	aacagcccct	tttaaaaagg	420
gaancantcc	tgntcttttc	caaatttt				448

<210> 89

<211> 463

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(463)

<223> n = A,T,C or G

<400> 89

gaattttgtg	cactggccac	tgtgatggaa	ccattggggc	aggatgcttt	gagtttatca	60
gtagtattc	tgccaaagtt	ggtgttgtaa	catgagtatg	taaaatgtca	aaaaattagc	120
agaggtctag	gtctgcatat	cagcagacag	tttgtccgtg	tattttgtag	ccttgaagtt	180
ctcagtgaca	agttntttct	gatgcgaagt	tctnattcca	gtgttttagt	cctttgcctc	240
tttnatgttn	agacttgcct	ctntnaaatt	gcttttgtnt	tctgcaggta	ctatctgtgg	300
tttaacaaaa	tagaannact	tctctgcttn	gaanatttga	atatcttaca	tctnaaaatn	360
aattctctcc	ccatannaaa	acccangccc	ttggganaat	ttgaaaaang	gntccttcnn	420
aattcnnana	anttcagntn	tcatacaaca	naacngganc	ccc		463

<210> 90
 <211> 400
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(400)
 <223> n = A,T,C or G

<400> 90
 agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt 60
 ctccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120
 tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctctccact 180
 tcctttgtta agacttcctc tggtaaagtc ttaagttttg tagaaaggaa ttttaattgct 240
 cgttctctaa caatgtcttc tccttgaagt atttggctga acaacccacc tnaagtcct 300
 ttgtgcatcc attttaaata tacttaatag ggcattggtn cactagggtta aattctgcaa 360
 ggtcatctg tctgcaaaag ttgcgttagt atatctgcca 400

<210> 91
 <211> 480
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(480)
 <223> n = A,T,C or G

<400> 91
 gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60
 ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac 120
 atgctctttt gactaccgtg tgccagtgtt ggtgattctc acacacctcc nccgctctt 180
 tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaat tcaccacga 240
 gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt 300
 tgtcaatact aaccgcgtgg tttgcctcca tcacatttgt gatctgtagc tctggataca 360
 tctcctgaca gtactgaaga acctcttctt ttgtttcaaa agcaactctt ggtgcctgtt 420
 ngatcagggt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa 480

<210> 92
 <211> 477
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(477)
 <223> n = A,T,C or G

<400> 92

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atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcgggtcact    60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt    120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggg    180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc    240
tgcagcgaaa ctctcgatg gtcattgagcg ggaagcgaat gangcccagg gccttgccca    300
gaaccttccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg    360
accagcggac aaacggcggt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc    420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg      477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (377)
<223> n = A,T,C or G

```

```

<400> 93
gaacggctgg accttgccctc gcattgtgct gctggcagga ataccttggc aagcagctcc    60
agtcagagca gccccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc    120
cgctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtg    180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa    240
caacaacaaa ataacatggt tgctgtttna gttgtataaa agtangtgat tctgtatnta    300
aagaaaatat tactgttaca tatactgctt gcaanttctg tattttattgg tncctctgaa    360
ataaatatat tattaata

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg ggttaggggc cagttcccag tggagaagaa aggccaggag aantgcgtgc    60
cgagctgang cagatttccc acagtgaacc cagagccctg ggctatagtc tctgacctct    120
ccaaggaaa accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg    180
gaaggcccca ttccgggggt gttccccgag gaggaaggga aggggctctg tgtgcccccc    240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa    300
tgcaagctca ccaagggtcc ctctcagtc ctccctaca ccctgaacgg nactggccc    360
acacccaccc agancancca cccgccatgg ggaatgttct caaggaatcg cngggcaacg    420
tggaactctg tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana    480
aaaaaaaaa aaaaaa

```

```

<210> 95
<211> 472

```


<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gccgaatttt 120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact 180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta 300
atcggcaaaa tgtggagtg atgttctttt cacagtaata tatgcctttt gtaacttcac 360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata 420
tttanttcan taatttcttt ccttgtttac gtttaattttg aaaagaatgc at 472

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

<400> 96
ctgaagcatt ttttcaaact tntctacttt tgtcattgat acctgtagta agttgacaac 60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt 120
ttttaactca tgactttttac acacacaatc cagaacttat tatatagcct ctaagtcttt 180
attcttcaca gtagatgatg aaagagtect ccagtgtctt gngcanaatg ttctagntat 240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat 300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
tacaaagtct atcttctctca nangtctgtn aaggaacaat ttaatcttct agcttt 476

<210> 97
<211> 479
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

<400> 97
actcttttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata 60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatagaa acacagctta 120

caatcgcaaa	tcaaaactca	caagtgtctca	tctgtttag	atttagtgta	ataagactta	180
gattgtgctc	cttcggatat	gattgtttct	canatcttgg	gcaatnttcc	ttagtcaa	240
caggctacta	gaattctgtt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnttttta	natcaaagta	ttttgtgttt	ggaantgtnn	aaatgaaatc	tgaatgtggg	420
ttcnatctta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tganccatc	479

<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

agtgacttgt	cctccaacaa	aaccccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtctc	tgtcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaaat	300
ttacctggag	aaaagagget	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgccggc	cgtttatgaa	ctgaccaccc	420
tttggaataa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

<210> 99

<211> 171

<212> DNA

<213> Homo sapien

<400> 99

gtggccgcgc	gcagggtgttt	cctcgctaccg	cagggccccc	tcccttcccc	aggcgtccct	60
cggcgccctct	gcgggcccga	ggaggagcgg	ctggcgggtg	gggggagtg	gaccacccct	120
cggtgagaaa	agccttctct	agcgatctga	gaggcgtgcc	ttgggggtac	c	171

<210> 100

<211> 269

<212> DNA

<213> Homo sapien

<400> 100

cggccgcaag	tgcaactcca	gctggggccg	tgccgacgaa	gattctgcca	gcagttggtc	60
cgactgcgac	gacggcggcg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaggtgagc	tgacgcgcga	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggg	gaagcgggag	gcctcgggga	gccccctggg	aagggcggcc	240
cgagagatac	gcagggtgcag	gtggccgcgc				269

<210> 101

<211> 405

<212> DNA

<213> Homo sapien

<400> 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttattttgca	60
------------	------------	------------	------------	------------	------------	----

gctagcaagg	taacagggtg	gggcatgggt	acatgttcag	gtcaacttcc	tttgtcgtgg	120
ttgattgggt	tgtctttatg	ggggcggggg	ggggtagggg	aaacgaagca	aataacatgg	180
agtgggtgca	ccctccctgt	agaacctggg	tacaaagctt	ggggcagttc	acctggctcg	240
tgaccgtcat	tttcttgaca	tcaatgttat	tagaagtcag	gatatctttt	agagagtcca	300
ctgttctgga	gggagattag	ggtttcttgc	caaatccaac	aaaatccact	gaaaaagttg	360
gatgatcagt	acgaataccg	aggcatattc	tcatatcggt	ggcca		405

<210> 102

<211> 470

<212> DNA

<213> Homo sapien

<400> 102

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ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaattt	aateccatta	tacggtatatt	120
tcaaaatcta	aattattcaa	atragccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
atatacttct	ttcagcaaac	ttgttacata	aattaaaaaa	atatatacgg	ctgggtgtttt	240
caaagtacaa	ttatcttaac	actgcaaac	ttttaaggaa	ctaaaataaa	aaaaaacact	300
ccgcaaaggt	taaagggaac	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttatatt	420
ttttaaacca	ttgtttgggc	ccaacacaat	ggaatcccc	ctggactagt		470

<210> 103

<211> 581

<212> DNA

<213> Homo sapien

<400> 103

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttatttttact	60
tacacatatt	tatttttat	aa	ttgggtattag	atattcaaaa	ggcagctttt	120
taaattggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgcttaaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	attttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaa	tatctaatct	ttccattttt	tccttattcc	aagtcaattt	300
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agggaaaaca	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaga	aggcttagat	ccttttatgt	480
ccatttttagt	cactaaacga	tatcaaagtg	ccagaatgca	aaagggttgt	gaacatttat	540
tcaaaagcta	atataagata	tttcacatac	tcactcttct	g		581

<210> 104

<211> 578

<212> DNA

<213> Homo sapien

<400> 104

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ctcttatgct	atatcatatt	ttaagttaaa	ctaagtgtgc	actggcttat	cttctcctga	180
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ttcatgcaaa	ctagaaaaata	atgtttcttt	tgcataagag	aagagaacaa	tatagcatta	360

caaaactgct	caaattgttt	gttaagttat	ccattataat	tagttggcag	gagctaatac	420
aatcacatt	tacgacagca	ataataaaac	tgaagtacca	gttaaataac	caaaataatt	480
aaaggaacat	ttttagcctg	ggtataatta	gctaattcac	tttacaagca	tttattagaa	540
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<210> 105

<211> 538

<212> DNA

<213> Homo sapien

<400> 105

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gtcttgaaca	ccaatattaa	tttgaggaaa	atacaccaaa	atacattaag	taaattattt	180
aagatcatag	agcttgtaag	tgaaaagata	aaatttgacc	tcagaaactc	tgagcattaa	240
aaatccacta	ttagcaataa	aattactatg	gacttcttgc	tttaattttg	tgatgaatat	300
ggggtgtcac	tggtaaacca	acacattctg	aaggatacat	tacttagtga	tagattctta	360
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ggcgagaaat	gaggaagaaa	agaaaaggat	tacgcatact	gttctttcta	tggaaggatt	480
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<210> 106

<211> 473

<212> DNA

<213> Homo sapien

<400> 106

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atttattagc	tctgcaactt	acatatltta	attaaagaaa	cgtttttagac	aactgtacaa	120
tttataaatg	taaggtgcc	ttattgagta	atatattcct	ccaagagtgg	atgtgtccct	180
tctcccacca	actaatgaac	agcaacatta	gtttaatttt	attagtagat	atacactgct	240
gcaaacgcta	attctcttct	ccatccccat	gtgatattgt	gtatatgtgt	gagttggtag	300
aatgcatcac	aatctacaat	caacagcaag	atgaagctag	gctgggcttt	cggtgaaaat	360
agactgtgtc	tgtctgaatc	aaatgatctg	acctatcctc	ggtggcaaga	actcttcgaa	420
ccgcttcctc	aaaggcgctg	ccacatttgt	ggctctttgc	acttgtttca	aaa	473

<210> 107

<211> 1621

<212> DNA

<213> Homo sapien

<400> 107

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ccgctacgac	gtgagccgct	tgggcccggg	caagcgctcg	ctagtgtctg	acctgaagca	180
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tggtgagaat	ccgtatgccc	cgctgaatct	cctggctgac	tttgctggtg	gtggccttat	480
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cattgatgca aatatgggtgg aaggaacagc atattttaagt tcttttctgt ggaaaactca 600
 gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatgggtg gagcaccttt 660
 ctatacgact tacaggacag cagatgggga attcatggct gttggagcaa tagaacccca 720
 gttctacgag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat 780
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 aatggttatc attagggtct ttgatttata aaactttggg tacttataact aaattatggg 1380
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 aaaagtcacg tgaaacaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaiaaaa aaaaaaaaaa 1620
 a 1621

<210> 108

<211> 382

<212> PRT

<213> Homo sapien

<400> 108

Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
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 20 25 30
 Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
 35 40 45
 Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
 50 55 60
 Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
 65 70 75 80
 Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
 85 90 95
 Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
 100 105 110
 Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
 115 120 125
 Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
 130 135 140
 Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
 145 150 155 160
 Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
 165 170 175
 Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
 180 185 190
 Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg

195	200	205
Gly Gln Asn Met Leu Asp	Gly Gly Ala Pro Phe Tyr	Thr Thr Tyr Arg
210	215	220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe		
225	230	235
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro		240
	245	250
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala		255
	260	265
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp		270
	275	280
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val		285
	290	295
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu		300
305	310	315
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Asn Thr Pro Ala		320
	325	330
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu		335
	340	345
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn		350
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Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu		365
370	375	380

<210> 109

<211> 1524

<212> DNA

<213> Homo sapien

<400> 109

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<210> 110

<211> 3410

<212> DNA

<213> Homo sapien

<400> 110

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<210> 111

<211> 1289

<212> DNA

<213> Homo sapien

<400> 111

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<210> 112

<211> 315

<212> PRT

<213> Homo sapien

<400> 112

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Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
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Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35      40      45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50      55      60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65      70      75      80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85      90      95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100      105      110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
115      120      125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130      135      140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145      150      155      160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165      170      175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180      185      190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu
195      200      205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
210      215      220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
225      230      235      240
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
245      250      255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
260      265      270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
275      280      285
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290      295      300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
305      310      315

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<210> 113

<211> 553

<212> PRT

<213> Homo sapien

<400> 113

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 Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val
 35 40 45
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
 50 55 60
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
 65 70 75 80
 Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
 85 90 95
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
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 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
 115 120 125
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
 130 135 140
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
 145 150 155 160
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
 165 170 175
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
 180 185 190
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
 195 200 205
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
 210 215 220
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
 225 230 235 240
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu
 245 250 255
 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
 260 265 270
 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
 275 280 285
 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
 290 295 300
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 305 310 315 320
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 325 330 335
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
 340 345 350
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
 355 360 365
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 370 375 380
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
 385 390 395 400
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
 405 410 415

Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
 420 425 430
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
 435 440 445
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser
 450 455 460
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
 465 470 475 480
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 485 490 495
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
 500 505 510
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
 515 520 525
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
 530 535 540
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala
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<210> 114

<211> 241

<212> PRT

<213> Homo sapien

<400> 114

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 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
 35 40 45
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
 50 55 60
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
 65 70 75 80
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
 85 90 95
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
 100 105 110
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
 115 120 125
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
 130 135 140
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
 145 150 155 160
 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
 165 170 175
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
 180 185 190
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
 195 200 205

Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
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 Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
 225 230 235 240
 Gln

<210> 115
 <211> 366
 <212> DNA
 <213> Homo sapien

<400> 115
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 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggt 240
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttaataaat tagtttggtg 300
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<210> 116
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 116
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 agactttact attttcatat tttaagacac atgatttatc ctatttttagt aacctgggtc 180
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<210> 117
 <211> 305
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(305)
 <223> n = A,T,C or G

<400> 117
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<210> 118
<211> 71
<212> DNA
<213> Homo sapien
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<400> 118

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<210> 119
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<212> DNA
<213> Homo sapien
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<400> 119

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<211> 90
<212> DNA
<213> Homo sapien
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 $\langle 400 \rangle$ 120

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<210> 121
<211> 218
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<212> DNA
<213> Homo sapien

<220>
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<223> n = A,T,C or G

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atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc 180
agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122
<211> 171
<212> DNA
<213> Homo sapien

<400> 122
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caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtcggt t 171

<210> 123
<211> 76
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(76)
<223> n = A,T,C or G

<400> 123
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ttatcaanta ttgtgt 76

<210> 124
<211> 131
<212> DNA
<213> Homo sapien

<400> 124
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ttaagatttg t 131

<210> 125
<211> 432
<212> DNA

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<213> Homo sapien

<400> 125
 actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg 60
 cttgaaaaag aggtgatagc tcttcagagg acttggtgact tttgctcaga tgctgaagaa 120
 ctacagtctg cttttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180
 ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240
 ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
 catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaattctcag 360
 caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcccttc 420
 ctctttgctt gt 432

<210> 126

<211> 112

<212> DNA

<213> Homo sapien

<400> 126
 acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact tcttaacct 60
 agtaagaatg atatttcccc ccagggatca ccaaataatt ataaaaattt gt 112

<210> 127

<211> 54

<212> DNA

<213> Homo sapien

<400> 127
 accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128

<211> 323

<212> DNA

<213> Homo sapien

<400> 128
 acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
 acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
 ttctctctga agtctagggt acccattttg gggaccatt ataggcaata aacacagttc 180
 ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240
 ttcttgcaaa aggctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
 aggtgcctt cttttccatg tcc 323

<210> 129

<211> 192

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(192)

<223> n = A,T,C or G

```

<400> 129
acatacatgt gtgtatatTT ttaaatatca cttttgtatc actctgactt tttagcatac      60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc      120
tagcacattc atctgtgata naaagatagg tgagtttcat ttctttcacg ttggccaatg      180
gataaacaaa gt                                     192

```

```

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(362)
<223> n = A,T,C or G

```

```

<400> 130
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca      60
tataatgacg caacaaaaag gtgctgttta gtcctatggg tcagtttatg cccctgacaa      120
gtttccattg tgttttgccg atcttctggc taatcgtggg atcctccatg ttattagtaa      180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata      240
cttattttaa agctcttatt ttgtggtcac taaaatggca atctatgtgc agcactttat      300
tgcagcagga agcacgtgtg ggttggttgt aaagctcitt gctaatttta aaaagtaatg      360
gg

```

```

<210> 131
<211> 332
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(332)
<223> n = A,T,C or G

```

```

<400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttggt ttaatggagt ttcccatgca      60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga      120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc      180
ttctgaacta gattaaggca gcttgtaa atctgatgtg ttggtttatt atccaactaa      240
cttccatctg ttatcactgg agaaagccca gactcccan gacnggtacg gattgtgggc      300
atanaaggat tgggtgaagc tggcgttgtg gt                                     332

```

```

<210> 132
<211> 322
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```


<223> n = A, T, C or G

acttttgcca	ttttgtatat	ataaacaatc	t.tgggacatt	ctcctgaaaa	ctaggtgtcc	60
agtggctaag	agaactcgat	ttcaagcaat	tctgaaagga	aaaccagcat	gacacagaat	120
ctcaaattcc	caaacagggg	ctctgtggga	aaaatgaggg	aggacctttg	tatctcgggg	180
tttagcaagt	taaaatgaan	atgacaggaa	aggcttattt	atcaacaaag	agaagagttg	240
ggatgcttct	aaaaaaaaact	ttggtagaga	aaataggaat	gctnaatcct	aggggaagcct	300
gtaacaatct	acaatttggtc	ca				322

<213> Homo sapien

<223> n = A, T, C or G

acaagccttc	acaagtttaa	ctaaattggg	attaatcttt	ctgtanttat	ctgcataatt	60
cttgtttttc	ttccatctg	gctcctgggt	tgacaatttg	tggaaacaac	tctattgcta	120
ctatttaaaa	aaaatcacaa	atctttccct	ttaagctatg	ttnaattcaa	actattcctg	180
ctattcctgt	tttgtcaaag	aaattatatt	tttcaaaata	tgntatttg	tttgatgggt	240
cccacgaaac	actaataaaa	accacagaga	ccagcctg			278

<213> Homo sapien

$\langle 223 \rangle$ n = A, T, C or G

```
gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaacttttcta ttttaaaaca      60
tgattctctg aggttaaact tggttttcaa atgttatatt tacttgcatt ttgccttttg      120
t                                                    121
```

<213> Homo sapien

<222> (1) ... (350)

<223> n = A,T,C or G

<400> 135
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60
 atancaagtg gtgactgggt aagcgtgcga caaagggtcag ctggcacatt acttgtgtgc 120
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtaactcca 180
 ggggtgcccc caactcctgc agccgctcct ctgtgccagn cctgnaagg aactttcgct 240
 ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgtgtgag 300
 ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccaggggtt 60
 gctgtgattg tatccgaata ntctcgtga gaaaagataa tgagatgacg tgagcagcct 120
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180
 cctggcgggc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag 240
 aaaactgcag agggccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgccac tggcggtgatg 360
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(165)

<223> n = A,T,C or G

<400> 137
 actggtgtgg tngggggtga tgctgggtgg anaagttgan gtgacttcan gatggtgtgt 60
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120
 ttggctggtc ccaactggtg tcactgtcat tgggtggggt cctgt 165

<210> 138

<211> 338

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<223> n = A, T, C or G

actcactgga	atgccacatt	cacaacagaa	tcagaggtct	gtgaaaaacat	taatggctcc	60
ttaacttctc	cagtaagaat	cagggacttg	aaatggaaac	gttaacagcc	acatgcccaa	120
tgctgggcag	tctcccatgc	cttcacagt	gaaagggctt	gagaaaaatc	acatccaatg	180
tcattgtgtt	ccagccacac	caaaaggtgc	ttgggggtgga	gggctggggg	catananggt	240
cangcctcag	gaagcctcaa	gttcatttca	gctttgccac	tgtacattcc	ccatntttta	300
aaaaactgat	gccttttttt	tttttttttg	taaaattc			338

<213> Homo sapien

gggaatcttg	gtttttggca	tctggtttgc	ctatagccga	ggccactttg	acagaacaaa	60
gaaagggact	tcgagtaaga	aggtgattta	cagccagcct	agtgccgaa	gtgaaggaga	120
attcaaacag	acctcgtcac	tccctgggtg	agcctggctg	gtccaccgcc	tatcatctgc	180
atttgcccta	ctcaggtgct	accggactcc	ggccctgat	gtctgtagtt	tcacaggatg	240
ccttattttg	cttctacacc	ccacagggcc	ccctacttct	tcggatgtgt	ttttaataat	300
gtcagctatg	tgcgccatcc	tccttcacgc	ccctccctcc	tttccctacca	ctgctgagtg	360
gcctggaact	tgtttaaagt	gt				382

<213> Homo sapien

<223> n = A,T,C or G

accaaancctt	ctttctggtt	tggtngattt	tactataggg	gtttngcttn	ttctaaanat	60
acttttcatt	taacancctt	tgtaaagtgt	caggctgcac	tttgctccat	anaattattg	120
ttttcacatt	tcaacttgta	tgtgtttgtc	tcttanagca	ttggtgaaat	cacatatttt	180
atattcagca	taaaggagaa					200

<213> Homo sapien

<223> n = A,T,C or G

<400> 141
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt 120
 atgcatgtag agaaccctaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180
 aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaaa agcaagatgg 300
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142
 <211> 459
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(459)
 <223> n = A,T,C or G

<400> 142
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60
 ggggttggtta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180
 cacatgggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240
 ttcaaacatc atagccaatg atgccccgct tgcttataat ctctccgaca taaaaccaca 300
 tcaacacctc agtgggccacc aaaccattca gcacagcttc ctttaactgtg agctgtttga 360
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420
 cagcangggg gggaggaacc agtcaacct tggcgtant 459

<210> 143
 <211> 140
 <212> DNA
 <213> Homo sapien

<400> 143
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120
 accatccgac ttcctgtgt 140

<210> 144
 <211> 164
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(164)
 <223> n = A,T,C or G

<400> 144
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaaattg 120

aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt

164

<210> 145
 <211> 303
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 145
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tccataacaa 60
 actggaggggt atttataccc aattatccca ttcattaaca tgccttcctc ctcaggctat 120
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca 180
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300
 caa 303

<210> 146
 <211> 327
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(327)
 <223> n = A,T,C or G

<400> 146
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60
 actggccttg agtgactcat tgctctgggt gggtgagaga gtccttttgc caacaggcct 120
 ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt 180
 cctgaacagg gaggggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc 240
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300
 taggggtgag ctgtgtgact ctatggt 327

<210> 147
 <211> 173
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(173)
 <223> n = A,T,C or G

<400> 147
 acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120

atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt 173

<210> 148
<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

<400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct 60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac 240
nccancccac ctccaccgacc ccatacctctt acacagctac ctcccttgctc tctaacccca 300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag 360
caccactggg aagccttctc cagccaacac acacacacac acacncacac acacacatat 420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg 477

<210> 149
<211> 207
<212> DNA
<213> Homo sapien

<400> 149
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60
taacgtatatt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180
tttcaggcag agggaacagc agtgaaa 207

<210> 150
<211> 111
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(111)
<223> n = A,T,C or G

<400> 150
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151
<211> 196
<212> DNA
<213> Homo sapien

<400> 151
 agcgcggcag gtcattatga acattccaga tacctatcat tactcgatgc tgttgataac 60
 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120
 ggataccaac cggaaaaccc ctatcccga cagcccactg tggccccac tgtctacgag 180
 gtgcattccg ctcagt 196

<210> 152
 <211> 132
 <212> DNA
 <213> Homo sapien

<400> 152
 acagcacttt cacatgtaag aaggagagaaa ttctaaatg taggagaaag ataacagAAC 60
 cttccccctt tcatttagtg gtggaaacct gatgctttat gttgacagga atagaaccag 120
 gagggagttt gt 132

<210> 153
 <211> 285
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(285)
 <223> n = A,T,C or G

<400> 153
 acaanaccca nganaggcca ctggccgtgg tgcattggcc tccaaacatg aaagtgtcag 60
 cttctgtctt tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120
 gcacatcaat aaagtccaaa gtcttggaact tggccttgcc ttggaggaag tcattcaaac 180
 cctggctagt gaggggtcgg cgccgtcct ggatgacggc atctgtgaag tcgtgcacca 240
 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285

<210> 154
 <211> 333
 <212> DNA
 <213> Homo sapien

<400> 154
 accacagtc tgttggggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60
 accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac 120
 cctaagccgg ttacacagct aactccact ggccctgatt tgtgaaattg ctgtgcctg 180
 attggcacag gagtcgaagg tgttcagctc cctcctcctg tggaaagaga ctctgattg 240
 agtttcacaa attctcgggc cacctcgtca ttgtcctct gaaataaaat ccggagaatg 300
 gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155
 <211> 308
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(308)
 <223> n = A,T,C or G

<400> 155
 actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg 60
 gaaagtgcct tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat 120
 ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180
 atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggt 240
 gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcattgctg 300
 gccttggt 308

<210> 156
 <211> 295
 <212> DNA
 <213> Homo sapien

<400> 156
 accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta 60
 ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaaactga 120
 gaataggaga ttatgtttgg cctcatatt ctctcctatc ctcccttgct cattctatgt 180
 ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat 240
 aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

<210> 157
 <211> 126
 <212> DNA
 <213> Homo sapien

<400> 157
 acaagtttaa atagtgtgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct 60
 gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc 120
 cttagt 126

<210> 158
 <211> 442
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(442)
 <223> n = A,T,C or G

<400> 158
 acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60
 aanccagcag gctgccccta gtcagtcctt ccttcagag aaaaagagat ttgagaaagt 120
 gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatat 180
 ctggtgggtc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta 240


```

natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg      300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga      360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg      420
tgttcattct ctgatgtcct gt                                         442

```

```

<210> 159
<211> 498
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(498)
<223> n = A,T,C or G

```

```

<400> 159
acttccaggt aacgttggtt tttccgttga gcctgaactg atgggtgacg ttgtaggttc      60
tccaacaaga actgaggttg cagagcgggt aggggaagagt gctgttccag ttgcacctgg      120
gctgctgtgg actggttggt attctctact acggcccaag gttgtggaac tggcanaaag      180
gtgtgttggt gganttgagc tcgggcggct gtggtaggtt gtgggctctt caacaggggc      240
tgctgtggtg ccgggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt      300
antanattct tcctgaaggc cagcgcctgt ggagctggca ngggtcantg ttgtgtgtaa      360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn      420
tcaggtaana atgtggtttc agtgtccctg ggngctgtg gaaggttgta nattgtcacc      480
aaggaataaa gctgtggt                                         498

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac      60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct      120
ggagcatggc atagaggaag ctganaaatg tggggctctga ggaagccatt tgagtctggc      180
cactagacat ctcatcagcc acttggtgta agagatgccc catgacccca gatgcctctc      240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg      300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa      360
cttgtagaat gaagcctgga                                         380

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161

```

actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca 60
cactgtccac tggccctta tccacttggg gcttaatccc tcgaaagagc atgt 114

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtthta atatcctcat atatatcaaa 60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120
tggatgata taacttggca ataaccagc ctggtgatac ataaaactac tcaactgt 177

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

<400> 163
catttataca gacagcggtg aagacattca cgacaaaaac gcgaaattct atcccgtagc 60
canagaaggc agctacggct actcctacat cctggcggtg gtggccttcg cctgcacctu 120
catcagcggc atgatgt 137

<210> 164
<211> 469
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(469)
<223> n = A,T,C or G

<400> 164
cttatcacia tgaatgttct cctgggcagc gttgtgatct ttgccacett cgtgacttta 60
tgcaatgcat catgctatth catacctaat gagggagttc caggagattc aaccaggaaa 120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt 180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgthtc tacacctgtg 240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg 300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct 360
tctagtaggc acagggtccc caggccaggc ctcatctccc tctggcctct aatagtcaat 420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacactth 469

<210> 165
<211> 195
<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgccgg	cacttgtgtt	cagtttcata	aagctgggtgg	60
atccgctgtc	atccactatt	ccttggctag	agtaaaaaatt	attccttatag	cccatgtccc	120
tgcaggccgc	ccgcccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcgga	gtccacacca	ccggtgtagg	tgtgtctaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgccaaac	tcgtctangg	tccgtgggaa	gctgggtgtcc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(247)

<223> n = A,T,C or G

<400> 167

acagagccag	accttggcca	taaatgaanc	agagattaag	actaaacccc	aagtccganat	60
tggagcagaa	actggagcaa	gaagtggggc	tggggctgaa	gtagagacca	aggccactgc	120
tatanccata	cacagagcca	actctcaggc	caaggcnatg	gttggggcag	anccagagac	180
tcaatctgan	tccaaagtgg	tggctggaac	actggtcatg	acanaggcag	tgactctgac	240
tgangtc						247

<210> 168

<211> 273

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(273)
<223> n = A,T,C or G

<400> 168
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg ttactttcaa 60
aatccctcan ccttggttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg 120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtgggc 180
aattcccaac ttcttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg 240
agtcccagat acactcatgg gctgccctgg gca 273

<210> 169
<211> 431
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A,T,C or G

<400> 169
acagccttgg ctcccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60
agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acagggttcta 120
ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacagggtgag 180
ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctgg gcaccagctc 300
acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatc atccaactgg 360
aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420
tcgaacactg a 431

<210> 170
<211> 266
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(266)
<223> n = A,T,C or G

<400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagtcca gaggtggagc 60
tcaaggagct ctgcaggcat tttgccaan cttctcanag canagggagc aacctacact 120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat 180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240
tcaaagctag ggggtctggca ggtgga 266

<210> 171
 <211> 1248
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(1248)
 <223> n = A,T,C or G

<400> 171
 ggcagccaaa tcataaacgg cgaggactgc agcccgccact cgcagccctg gcaggcggca 60
 ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcacccgca gtgggtgctg 120
 tcagccgcac actgtttcca gaagtgaagt cagagctcct acaccatcgg gctgggcctg 180
 cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta 240
 cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac 300
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgcctacc 360
 gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420
 gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac 480
 ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc 540
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgct acaccaacct ctgcaaattc 660
 actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aaccatgaa 720
 attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccctcct 780
 cctcaggcc caggagtcca gggcccagc cctcctccc tcaaaccaag ggracagatc 840
 cccagccct cctccctcag acccaggagt ccagaccccc cagccctcc tccctcagac 900
 ccaggagtcc agccctcct cctcagacc caggagtcca gacccccag cccctcctcc 960
 ctcagaccca ggggtccagg cccccaacct ctctccctc agactcagag gtccaagccc 1020
 ccaaccntc attccccaga cccagaggtc cagggtccag cccctcntcc ctcagaccca 1080
 gcggtccaat gccacctaga ctntccctgt acacagtgcc ccttgtggc acgttgaccc 1140
 aacctacca gttggttttt catTTTTngt ccctttccc tagatccaga aataaagttt 1200
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172
 <211> 159
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(159)
 <223> Xaa = Any Amino Acid

<400> 172
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1 5 10 15
 Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
 20 25 30
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
 35 40 45

Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
 50 55 60
 Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
 65 70 75 80
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
 85 90 95
 Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
 100 105 110
 Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
 115 120 125
 Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
 130 135 140
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 145 150 155

<210> 173

<211> 1265

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(1265)

<223> n = A,T,C or G

<400> 173

ggcagccccgc	actcgcagcc	ctggcaggcg	gcactgggtca	tggaaaaacga	attgttctgc	60
tggggcgctcc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacaactgttt	ccagaactcc	120
tacaccatcgc	ggctgggcct	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gaccttgct	cgctaacgac	240
ctcatgctca	tcaagttgga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgccctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggaggtcctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgcgccccag	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggg	ggtgtctgag	gaggtctgca	gtaagctcta	tgaccgctg	taccacccca	540
gcattgtctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggt	gactctgggg	600
ggccctgat	ctgcaacggg	tacttgagg	gccttggtgc	tttcggaaaa	gccccgtgtg	660
gccaagttgg	cgtgccaggt	gtctacacca	acctctgcaa	attcactgag	tggatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaaattgac	ccccaaatac	780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcctccctca	ggcccaggag	840
tccaggcccc	cagccctcc	tccctcaaac	caagggtaca	gatccccagc	ccctcctccc	900
tcagaccag	gagtccagac	ccccagcccc	ctctccctc	agaccagga	gtccagcccc	960
tcctccntca	gaccagagg	tccagacccc	ccagccctc	ctccctcaga	cccaggggtt	1020
gaggccccca	acccctcctc	cttcagagtc	agagggtcaa	gcccccaacc	cctcggtccc	1080
cagaccaga	ggttnaggtc	ccagccctc	ttccntcaga	cccagnggtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggngangtg	acccaacctt	accagttggt	1200
ttttcatttt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

<210> 174

<211> 1459

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1459)
<223> n = A,T,C or G

<400> 174

```

ggtcagccgc acactgtttc cagaagtggag tgcagagctc ctacaccatc gggctggggc      60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg      120
tacggcaccr agagtacac acacccctgc tcgctaacga cctcatgctc atcaagttgg      180
acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgtctcg cagtgcctta      240
ccgcggggaa ctcttgccct gtttctggct ggggtctgct ygcgaacggg gagctcacgg      300
gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct      360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgctg aacgctgctg tgggtgtctga      420
ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgcggggcg      480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact      540
caggggaagg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag      600
atggagagac acacagggag acagtgacaa cttagagagag aaactgagag aaacagagaa      660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc      720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggt      780
gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaaa ctgactagaa      840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgaltt atgcatacgt      900
tttatgcatt catgatatac ctttgttggg attttttgat atttctaagc tacacagttc      960
gtctgtgaat ttttttaaat tgttgcaact ctcttaaaat ttttctgarg tgtttattga     1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaacigt     1080
gtaccacagag ggaacacagt acacagattc atagaggtga aacacgaaga gaaacaggaa     1140
aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaate ccagcacttt     1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaarg     1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt     1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt     1380
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct     1440
caaaaaaaaa aaaaaaaaaa

```

<210> 175
<211> 1167
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1167)
<223> n = A,T,C or G

<400> 175

```

gcgcagccct ggcaggcggc actgggtcatg gaaaacgaat tgttctgctc gggcgtcctg      60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg      120
ctgggcctgc acagtcttga ggccgaccaa gagccagga gccagatggg ggaggccagc      180
ctctccgtac ggcaccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc      240
aagttggacg aatccgtgtc cgagtctgac accatccgga gcacagcat tgcttcgcag      300

```

```

tgcctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360
atgcctaccg tgctgcactg cgtgaacgtg tccgtggtgt ctgaggangt ctgcagtaag 420
ctctatgacc cgctgtacca cccagcatg tctgcgcgcg gcggagggca agaccagaag 480
gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgteta caccaacctc 600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga 660
acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720
gcccctctc cctcaggccc aggagtccag gccccagcc cctcctccct caaaccaagg 780
gtacagatcc ccagccctc ctcctcaga cccaggagtc cagacccccc agcccctcnt 840
ccntcagacc caggagtcca gcccctctc cntcagacgc aggagtccag acccccagc 900
ccntcntccg tcagaccag ggggtcaggc ccccaacccc tcntccntca gagtccagag 960
tccaagcccc caaccctcg tccccagac ccagaggtn cagggtcccag cctcctccc 1020
tcagaccag cgggtccaatg ccacctagan tntccctgta cacagtgcgc ccttgtggca 1080
ngttgacca acctaccag ttgggttttc attttttgtc cctttccctt agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa 1167

```

<210> 176

<211> 205

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1) ... (205)

<223> Xaa = Any Amino Acid

<400> 176

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1           5           10           15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
          20           25           30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
          35           40           45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
          50           55           60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65           70           75           80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
          85           90           95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
          100          105          110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
          115          120          125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
          130          135          140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145          150          155          160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
          165          170          175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
          180          185          190

```


Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
 195 200 205

<210> 177
 <211> 1119
 <212> DNA
 <213> Homo sapien

<400> 177

```

gcgcactcgc agccctggca ggcggcactg gtcattgaaa acgaattggt ctgctcgggc 60
gtccttggtgc atccgcagtg ggtgctgtca ggcgcacact gtttcagaaa ctccacacc 120
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag 180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300
tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctggggtct gctggcgaac 360
gatgctgtga ttgccatcca gtccagact gtgggaggct gggagtgtga gaagctttcc 420
caaccctggc aggggtgtac catttcggca acttcagtg caaggacgtc ctgctgcac 480
ctcactgggt gctcactact gctcactgca tcaccggaa cactgtgatc aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctgggtact cctccacaaa 780
ttcatttctc ctgttgtagt gaaagggtgc ccctctggag cctcccaggg tgggtgtgca 840
ggtcacaaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg 900
ctcagtacac cagggcaggt ctacgatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgact agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggaatctgtc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa 1119

```

<210> 178
 <211> 164
 <212> PRT
 <213> Homo sapien

<220>
 <221> VARIANT
 <222> (1)...(164)
 <223> Xaa = Any Amino Acid

<400> 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1           5           10           15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
          20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
          35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
          50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly

```

	85		90		95
Asn Ser Cys	Leu Val Ser Gly Trp Gly	Leu Leu Ala Asn Asp Ala Val			
	100		105		110
Ile Ala Ile	Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu				
	115		120		125
Ser Gln Pro	Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg				
	130		135		140
Thr Ser Cys	Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser				
	145		150		155
Pro Gly Thr	Leu				160

<210> 179

<211> 250

<212> DNA

<213> Homo sapien

<400> 179

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct	60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct	120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga	180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa	240
aaaaaaaaaa	250

<210> 180

<211> 202

<212> DNA

<213> Homo sapien

<400> 180

actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca	60
tcacccagac ccgccccctg cccgtgcccc acgtgctgc taacgacagt atgatgctta	120
ctctgctact cggaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc	180
tgatttaaaa aaaaaaaaaa aa	202

<210> 181

<211> 558

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(558)

<223> n = A,T,C or G

<400> 181

tcyytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg	60
aatgtttagg cagtgctagt aatttcytcg taatgattct gttattactt tcctnattct	120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa	180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca	240
aaattatgca agtttagtaat tactcagggt taactaaatt actttaatat gctgttgaac	300

```

ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540
caaaaaaaaa aaaaaaaaaa 558

```

```

<210> 182
<211> 479
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

```

```

<400> 182
acagggwttk grggatgcta agsccccrga rwtggttga tccaaccctg gcttwttttc 60
agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120
cstcacacag astcccagat agctgggact acaggcacac agtcactgaa gcaggccctg 180
ttwgcattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca 300
tactmttcta agtctctctc cagctcact kkgagtcctm rytgggggtt gataggaent 360
ntctcttggc ttcttcaata aartctctat ycatctcatg ttttaatttg tadgcatara 420
awtgscgara aaattaaaat gttctggtty macttcaaaa aaaaaaaaaa aaaaaaaaaa 479

```

```

<210> 183
<211> 384
<212> DNA
<213> Homo sapien

```

```

<400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60
agtaccagta ccaataacag tgccagtgcg agtgccagca ccagtgggtg cttcagtgc 120
ggtgccagcc tgaccgccac tctcacattt gggtctcttg ctggccttgg tggagctgg 180
gccagcacca gtggcagctc tgggtgcctgt gggttctcct acaagtgaga ttttagatat 240
tgtaaatcct gccagtcttt ctcttcaagc cagggtgcac cctcagaaac ctactcaaca 300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360
gccatttcaa aaaaaaaaaa aaaa 384

```

```

<210> 184
<211> 496
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(496)
<223> n = A,T,C or G

```

```

<400> 184

```

```

accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatcac ctcaacgagc 60
aggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag 120
cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180
aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac 240
tgatgtcttt tctgccacct gttacccttc ggagactccg taaccaaact cttcggactg 300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg 360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt 420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst 480
taaaaaaaaa aaaaaa 496

```

<210> 185

<211> 384

<212> DNA

<213> Homo sapien

<400> 185

```

gctggtagcc tatggcgkgg ccacaggagg ggctcctgag gccacggrac agtgacttcc 60
caagtatcyt gcgcsgegtc ttctaccgtc cctacctgca gatcttcggg cagattcccc 120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct 180
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg 240
tggtgctgct cctcgtcatt ttctgctcg tggccaacat cctgctggtc aacttgctca 300
ttgccatggt cagttacaca ttcggcaaag tacagggcaa cagcgatctc tactgggaag 360
gcgcagcgtt accgectcat ccgg 384

```

<210> 186

<211> 577

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(577)

<223> n = A,T,C or G

<400> 186

```

gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt 120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttcgc 180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt 240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac 300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttggtgtg gggkkgaa 360
ctcaccacaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgcccag 420
gtggaaaaaag amcamctcct ggargtgctn gccgctctc gtcmgttggg ggcagcgtw 480
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540
aagatntcgc acagcactna tccagttggg attaaat 577

```

<210> 187

<211> 534

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(534)
 <223> n = A,T,C or G

<400> 187

aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgstg	agaatycatw	60
actkggaaaa	gmaacattaa	agcctggaca	ctgggtattaa	aattcacaat	atgcaacact	120
ttaaacagtg	tgtcaatctg	ctcccyynac	tttgtcatca	ccagtctggg	aakaagggta	180
tgccctattc	acacctgtta	aaagggcgct	aagcatcttt	gattcaacat	cttttttttt	240
gacacaagtc	cgaaaaaagc	aaaagtaaac	agttatyaat	ttgttagcca	attcactttc	300
ttcatgggac	agagccatyt	gatttaaaaa	gcaaattgca	taatattgag	cttygggagc	360
tgatatttga	gcggaagagt	agcctttcta	cttcaccaga	cacaactccc	tttcatattg	420
ggatgttnac	naaagtwatg	tctctwacag	atgggatgct	tttgtggcaa	ttctgttctg	480
aggatctccc	agtttattta	ccacttgcac	aagaaggcgt	tttcttcttc	aggg	534

<210> 188
 <211> 761
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(761)
 <223> n = A,T,C or G

<400> 188

agaaaccagt	atctctnaaa	acaacctctc	ataccttggtg	gacctaat	ttgtgtgcgtg	60
tgtgtgtgcg	cgcatattat	atagacaggc	acatcttttt	tacttttcta	aaagcttatg	120
cctcttttgg	atctatatct	gtgaaagt	taatgatctg	ccataatgtc	ttggggacct	180
ttgtcttctg	tgtaaatggt	actagagaaa	acacctatnt	tatgagtcaa	tctagttngt	240
ttttattcga	atgaaggaaa	tttcagatn	acaacactna	caaactctcc	ctkgackarg	300
ggggacaaag	aaaagcaaaa	ctgamcataa	raaacaatwa	cctggtgaga	arttgcataa	360
acagaaatwr	ggtagtatat	tgaarnacag	catcattaaa	rmgtttwtktt	wtctctccctt	420
gcaaaaaaca	tgtacngact	tcccgttgag	taatgccaa	ttgttttttt	tatnataaaa	480
cttgcccttc	attacatggt	tnaaagtgg	gtgggtggg	aaaatattga	aatgatggaa	540
ctgactgata	aagctgtaca	aataagcagt	gtgcctaaca	agcaacacag	taatgttgac	600
atgcttaatt	cacaaatgct	aatttcatta	taaagtgttg	ctaaaataca	ctttgaacta	660
ttttctctgn	ttcccagagc	tgagatntta	gattttatgt	agtatnaagt	gaaaaantac	720
gaaaataata	acattgaaga	aaaananaaa	aaanaaaaaa	a		761

<210> 189
 <211> 482
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(482)
 <223> n = A,T,C or G

<400> 189

```

tttttttttt tttgcccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca      60
caccgggggt atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca      120
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc      180
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggagtgt gcataagaag      240
tgataggcac aggccacccg gtacagaccc ctcggtcct gacaggtnga tttcgaccag      300
gtcattgtgc cctgcccagg cacagcgta atctggaaaa gacagaatgc tttccttttc      360
aaatttggct ngtcatngaa ngggcanttt tccaantng gctnggtctt ggtacncttg      420
gttcggccca gctcncgct caaaaantat tcacconnet ccnaattgct tgcnggnccc      480
cc

```

<210> 190

<211> 471

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(471)

<223> n = A,T,C or G

<400> 190

```

tttttttttt ttttaaaaca gtttttcaca acaaaaattta ttagaagaat agtgggttttg      60
aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtnctcca      120
aatgtctggg caaatgatac aatggaacca ttcaatctta cacatgcagg aaagaacaag      180
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg atraaaaattt      240
taagtactca tcacatacat taagacacag ttctaqtcca gtcnaaaatc agaactgcnt      300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta      360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaaanaa      420
tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c

```

<210> 191

<211> 402

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(402)

<223> n = A,T,C or G

<400> 191

```

gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct      60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa      120
attcttcacc agtcacatct tctaggacct ttttgattc agttagtata agctcttcca      180
cttcctttgt taagacttca tctggtaaaag tcttaagttt tgtagaaagg aattyaattg      240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc      300
ctttgtgcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc      360
aagagtcacg tgtctgcaaa agttgcgtta gtatatctgc ca

```

<210> 192

<211> 601
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(601)
 <223> n = A,T,C or G

<400> 192

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact	60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac	120
atgcytyttt gaytaccgtg tgccaagtgc tgggtgattct yaacacacyt ccatcccggt	180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcacc	240
acgagacact tgaaaggtgt aacaaagcga ytcttgcaatt gctttttgtc cctccggcac	300
cagttgtcaa tactaaccgc ctgggtttgcc tccatcacat ttgtgatctg tagctctgga	360
tacatctect gacagtactg aagaacttct tcttttgttt caaaagcacc tcttggtgcc	420
tggtggatca gggtccatt tcccagtcyg aatgttcaca tggcatatct wacttcccac	480
aaaacattgc gattttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag	540
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag ccccaccagc agcagaagca	600
g	601

<210> 193
 <211> 608
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(608)
 <223> n = A,T,C or G

<400> 193

atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcgggtcact	60
ggtcccgcgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt	120
ccccacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg	180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccagc tgtgcgggac	240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggcttgccc	300
agaaccttcc gctgtttctc tggcgctcac tgcagctgct gccgctgaca ctccggcctcg	360
gaccagcgga caaacggcrt tgaacagccg cacttcacgg atgcccagtg tgtcgcgctc	420
caggammgsc accagcgtgt ccagggtcaat gtccgtgaag ccctccgcgg gtrattggcgt	480
ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga	540
gtcgcgcttg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcagggaactc	600
cacgcaat	608

<210> 194
 <211> 392
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(392)
 <223> n = A,T,C or G

<400> 194
 gaacggctgg accttgccctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt 60
 ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccctcccc 120
 tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg 180
 tttgatttta cttgggaatt tcctctgita tatagctttt cccaatgcta atttccaaac 240
 aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt 300
 taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg 360
 aaataaatat agttattaaa ggtgtcant cc 392

<210> 195
 <211> 502
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(502)
 <223> n = A,T,C or G

<400> 195
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60
 ccgagctgag gcagatgttc ccacagtga cccagagcc stgggstata gtytctgacc 120
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180
 aaggaaggc cccattccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc 240
 ccccasgagg aagagggcct gagtcctggg atcagacacc ccttcacgtg tatccccaca 300
 caaatgcaag ctccaccaagg tccccctctca gtcccccttc stacaccctg amcgccact 360
 gscscacacc caccagagc acgccaccg ccattggggar tgtgtcaag gartcgcnng 420
 gcarcgtgga catctngtcc cagaagggg cagaatctcc aatagangga ctgarcmstt 480
 gctnanaaaa aaaaanaaaa aa 502

<210> 196
 <211> 665
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(665)
 <223> n = A,T,C or G

<400> 196
 ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120
 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180
 actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc 240
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300
 attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360


```

tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatgggtatgt      420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt      480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt      540
ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac      600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan      660
aagtg

```

```

<210> 197
<211> 492
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

```

```

<400> 197
ttttnttttt ttttttttgc aggaaggatt ccattttattg tggatgcatt ttcacaatat      60
atgttttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg      120
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag      180
aatttatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta cctgaaact tactccatcc aaatattgga ataanagtca gcagtgtac      300
attctcttct gaacttttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcaact ccatcacggg agtcaatgct acctgggaca cttgtatttt gtcatnctg      480
ancntggctt aa

```

```

<210> 198
<211> 478
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(478)
<223> n = A,T,C or G

```

```

<400> 198
ttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngattht aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnc      420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa      478

```

```

<210> 199
<211> 482
<212> DNA

```

seq#123456789

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagttcc	tgtcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttctctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggctttngg	ctggggacca	tcccattgaa	ccttctctta	360
anggacttta	agaanaaaact	accacatgtn	tgtngtatcc	tgggtgccngg	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcttgaactt	gctcctctgc	480
ga						482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(270)

<223> n = A,T,C or G

<400> 200

cggccgcaag	tgcaactcca	gctggggccg	tgccgacgaa	gattctgcca	gcagttggtc	60
cgactgcgac	gacggcgccg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaagctgagc	tgacgccgca	gaggtcgtgt	cacgtccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggg	gaangcgggg	ggcctcgggg	agccccctcg	gaagggcgcc	240
ccgagagata	cgcaggtgca	ggtggccgcc				270

<210> 201

<211> 419

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(419)

<223> n = A,T,C or G

<400> 201

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttatttttgca	60
gctagcaagg	taacagggtg	gggcatgggt	acatgttcag	gtcaacttcc	tttgtcgtgg	120
ttgattgggt	tgtctttatg	ggggcggggt	ggggtagggg	aaancgaagc	anaantaaca	180
tggagtgggt	gcaccctccc	tgtagaacct	ggttacnaaa	gcttggggga	gttcacctgg	240
tctgtgaccg	tcattttctt	gacatcaatg	ttattagaag	tcaggatatc	ttttagagag	300

tccactgtnt ctggagggag attagggttt cttgccana tccaancaaa atccacntga 360
 aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cgggtggcca 419

<210> 202
 <211> 509
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 202
 tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatnenc cattatacng 120
 gtnattttnc aaaatctaaa nmttattcaa atntnagcca aantccttac ncaaatnnaa 180
 tacnncaaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa 240
 aatatatacg gctgggtgtt tcaaagtaca attatcttaa cactgcaaac atnttttnaa 300
 ggaactaaaa taaaaaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360
 caacancnnc nattataaaa atcatatctc aaatccttagg ggaatatata cttcacacng 420
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480
 caatggnaat nccnccnncn tggactagt 509

<210> 203
 <211> 583
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(583)
 <223> n = A,T,C or G

<400> 203
 tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttatttttact 60
 tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120
 taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgccataaagt 180
 gaaaaatctt tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240
 atttttcttg tcttttaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300
 gcttctctag cctcatattc tagctcttat ctactattag taagtggctt ttttcctaaa 360
 agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc 420
 tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tctttttatg 480
 tccatttttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540
 attcaaaagc taatataaga tatttcacat actcatcttt ctg 583

<210> 204
 <211> 589
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(589)
 <223> n = A,T,C or G

<400> 204
 tttttttnt ttttttttt ttttttntc ttcttttttt ttganaatga ggatcgagtt 60
 tttcactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca 120
 aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180
 tgaaggaaat ctgttcattc ttctcattca tatagttara tcaagtacta ccttgcatat 240
 tgagaggttt ttcttctcta ttacacata tatttccatg tgaatttgta tcaaacccttt 300
 attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag 360
 cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag 420
 ctaatacaaaa tcacatttac ngacnagcaa taataaaaact gaagtaccag ttaaatatcc 480
 aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat 540
 ttattnagaa tgaattcaca tgttattatt cntagccca acacaatgg 589

<210> 205
 <211> 545
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(545)
 <223> n = A,T,C or G

<400> 205
 tttttntttt ttttttcagt aataatcaga acaatattta tttttaratt taaaattcat 60
 agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120
 tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaaattat 180
 ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240
 aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300
 atgggggtgc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360
 tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420
 aaggggcnaga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatnng 480
 aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540
 aaccc 545

<210> 206
 <211> 487
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(487)
 <223> n = A,T,C or G

<400> 206
 tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60

```

catttattag ctctgcaact tacatatatta aattaaagaa acgttnttag acaactgtna      120
caatttataa atgtaagggt ccattattga gtanatatat tctccaaga gtggatgtgt      180
cccttctccc accaactaat gaancagcaa cattagttaa attttattag tagatnatac      240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag      300
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt      360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag      420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt      480
ttcaaaa

```

<210> 207

<211> 332

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature ;

<222> (1)...(332)

<223> n = A,T,C or G

<400> 207

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tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cttttaaaaa      60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact      120
gcatttarag gaccttctgg tggttctgct gttacncttg aantctgaca atccttgana      180
atctttgcat gcagaggagg taaaagggtat tggattttca cagagggaana acacagcgca      240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg      300
aaaagaaggc agcctaggcc ctggggagcc ca

```

<210> 208

<211> 524

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(524)

<223> n = A,T,C or G

<400> 208

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agggcgtggt gcggaggggc ttactgtttt gtctcagtaa caataaatac aaaaagactg      60
gttgtgttcc ggcccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat      120
tttaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac      180
tccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact      240
tttggcagaa tacttnttga aacttgcaaga tgataactaa gatccaagat atttcccaaa      300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc      360
atgagcccag acactgacat caaactaagc ccacttagac tctcaccac cagtctgtcc      420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa      480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga

```

<210> 209

<211> 159

<212> DNA

<213> Homo sapien

<400> 209
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120
 caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

<210> 210

<211> 256

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(256)

<223> n = A,T,C or G

<400> 210
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120
 tggggagatt ctanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180
 ttgcaggggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240
 ccaggatgct aatca 256

<210> 211

<211> 264

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(264)

<223> n = A,T,C or G

<400> 211
 acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60
 actggaacac ataccacat ctttgttctg aggataatt ttctgataaa gtcttgctgt 120
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240
 aaaaaaggag caaatgagaa gcct 264

<210> 212

<211> 328

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 212
 acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa 60
 ggatttaaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180
 ttnaatttca ttccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta 240
 cccctacnac tctttactct ctgganaggg ccagtgggtgg tagctataag cttggccaca 300
 ttttttttct ctttattcct ttgtcaga 328

<210> 213
 <211> 250
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(250)
 <223> n = A,T,C or G

<400> 213
 acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
 cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatata tctctnacct 240
 tctcatcggt 250

<210> 214
 <211> 444
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(444)
 <223> n = A,T,C or G

<400> 214
 acccagaatc caatgctgaa tatttggcct cattattccc agattctttg attgtcaaag 60
 gatttaaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg 120
 tttatatatg cagcaacaat attcaagcgc gacaacagggt tattgaactt gcccgccagt 180
 tgaattttcat tccatttgac ttgggatcct tatcatcagc canagagatt gaaaatttac 240
 ccctacgact ctttactctc tggagagggc cagtgggtgg agctataagc ttggccacat 300
 ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag 360
 agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt 420
 actttgctct cccaatata cctc 444

<210> 215
 <211> 366
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(366)
 <223> n = A,T,C or G

<400> 215
 acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt 60
 taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct 120
 cattatgcc aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt 180
 ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatata tctctgacct 240
 tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa 300
 tccaagctgt tttctacact gtaaccagggt ttccaaccaa ggtggaaatc tcctatactt 360
 ggtgcc

<210> 216
 <211> 260
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(260)
 <223> n = A,T,C or G

<400> 216
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120
 taataaaaag tnnaaaaggc ctcttctcaa ctttttcccc ttnggctgga aaatttaaaa 180
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240
 aattcttctt tccctccttt

<210> 217
 <211> 262
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(262)
 <223> n = A,T,C or G

<400> 217
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60
 tcttgcttat aattttctat ttttaataagg aaatagcaaa ttgggggtggg gggaatgtag 120
 ggcatcttac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt 180
 atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta 240
 atatccttca tgcttgtaaa gt 262

<210> 218
 <211> 205
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(205)
 <223> n = A,T,C or G

<400> 218
 accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca 60
 cccctatcaa ctcccttttg tagtaaacctt ggaaccttgg aaatgaccag gccaaagactc 120
 aggcctcccc agttctactg acctttgtcc ttangtntna ngcccagggt tgctaggaaa 180
 anaaatcagc agacacaggt gtaaa 205

<210> 219
 <211> 114
 <212> DNA
 <213> Homo sapien

<400> 219
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gcccattcca 60
 accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220
 <211> 93
 <212> DNA
 <213> Homo sapien

<400> 220
 actagccagc acaaaaggca gggtagcctg aattgcttcc tgctctttac atttctttta 60
 aaataagcat ttagtgctca gtcctactg agt 93

<210> 221
 <211> 167
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(167)
 <223> n = A,T,C or G

<400> 221
 actangtgca ggtgcgcaca aatatttgtc gatattccct tcattcttga ttccatgagg 60
 tcttttgccc agcctgtggc tctactgtag taagtctctg ctgatgagga gccagnatgc 120
 cccccactac ctccctgac gctcccana aatcacccaa cctctgt 167

<210> 222
 <211> 351
 <212> DNA
 <213> Homo sapien

<400> 222

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agggcggtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc      60
gttcttcacc tgtcccccac tccttaaaag gccatactgc ataaagtcaa caacagataa      120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa      180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt      240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt      300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t                351

```

<210> 223

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 223

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aaaaacaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat      60
tggttaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga      120
ttaaaatgtc tgtgccaaaa ttttgatttt tatttgagga cttcttatca aaagtaatgc      180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttgagg tgtgctattc      240
taaaagattt tgatttcctg gaatgacaat tatattttta ctttggtggg ggaaanagtt      300
ataggaccac agtcttcact tctgatactt gtaaattaat cttttattgc acttgttttg      360
accattaage tatatgttta aaa                383

```

<210> 224

<211> 320

<212> DNA

<213> Homo sapien

<400> 224

```

ccctgaagg cttcttggtta gaaaatagta cagttacaac caataggaac aacaaaaaga      60
aaaagtttgt gacattgtag tagggagtgt gtaccctta ctcccatca aaaaaaaaat      120
ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa      180
gagaaaatac tactttctcr aaatggaagc ctttaaaggt gctttgatac tgaaggacac      240
aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgrrgcagt      300
tttaractcm gcattgtgac                    320

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<210> 225

<211> 1214

<212> DNA

<213> Homo sapien

<400> 225

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gaggactgca gcccgcactc gcagccctgg caggcggcac tggtcatgga aaacgaattg      60
ttctgctcgg gcgtcctggt gcatccgcag tgggtgctgt cagccgcaca ctgtttccag      120
aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc      180
cagatgggtg aggccagcct ctccgtacgg caccagagt acaacagacc cttgctcgct      240
aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc      300
atcagcattg cttegcagtg cctaccgcg gggaactctt gcctcgtttc tggctggggg      360

```

ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	tgaacgtgtc	ggtgggtgtct	420
gaggaggtct	gcagtaagct	ctatgaccgg	ctgtaccacc	ccagcatggt	ctgcgccggc	480
ggagggcaag	accagaagga	ctcctgcaac	ggtgactctg	ggggggccct	gatctgcaac	540
gggtacttgc	agggccttgt	gtctttcgga	aaagccccgt	gtggccaagt	tggcgtgcc	600
ggtgtctaca	ccaacctctg	caaattcact	gagtggatag	agaaaaaccgt	ccaggccagt	660
taactctggg	gactgggaac	ccatgaaatt	gacccccaaa	tacatcctgc	ggaaggaatt	720
caggaatata	tgttcccagc	ccctcctccc	tcaggcccag	gagtcagggc	ccccagcccc	780
tcctccctca	aaccaagggt	acagatcccc	agccctcctc	ccctcagacc	caggagtcca	840
gacccccag	ccctcctccc	ctcagaccga	ggagtcaggc	ccctcctccc	tcagaccccag	900
gagtcagac	ccccagccc	ctcctccctc	agacccaggg	gtccaggccc	ccaacccctc	960
ctccctcaga	ctcagagggt	caagccccc	acccctcctc	ccccagacc	agagggtccag	1020
gtcccagccc	ctcctccctc	agacccagcg	gtccaatgcc	acctagactc	tccctgtaca	1080
cagtgcctcc	ttgtggcacg	ttgacccaac	cttaccagtt	ggtttttcat	tttttgtccc	1140
tttcccttag	atccagaaat	aaagtctaag	agaagcgcaa	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaa					1214

<210> 226

<211> 119

<212> DNA

<213> Homo sapien

<400> 226

acccagtagt	tgcagggaga	cggaacccca	tgtgacagcc	cactccacca	gggttcccaa	60
agaacctggc	ccagtcataa	tcattcatcc	tgacagtggc	aataatcacg	ataaccagt	119

<210> 227

<211> 818

<212> DNA

<213> Homo sapien

<400> 227

acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggctctccc	ccagccctga	60
tttttgctac	atatgggggc	ccttttcatt	ctttgcaaaa	acactgggtt	ttctgagaac	120
acggacggtt	cttagcacia	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcttc	ctctggagga	aagggtggtg	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgtcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgctccc	ttccaatcag	ccactttctg	gaacccccat	ctaacttctc	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaagggtg	cacctcagc	agagaagccg	agagcttaac	tctggctcgt	tccagagaca	480
acctgctggc	tgtcttggga	tgcgcccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcattgagagg	600
gacaggctct	gcctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	agggttttcag	cctagatggg	agtcgtgt			818

<210> 228

<211> 744

<212> DNA

<213> Homo sapien

<400> 228

actggagaca	ctggtgaact	tgatcaagac	ccagaccacc	ccagggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggaagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcactgt	ggaactacca	aatggcgaga	240
tgctcgggtgc	acattgggggt	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtcc	acctctgcag	360
gctggcagct	gaatggcttg	ccggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaata	cacaggcgcc	ctcctgggtga	cagtgacccg	540
ccgtgggtatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttgggggtttg	600
ttcttttcgt	taatgttctc	ctgtgttgct	agctgtcttc	atttcttggg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttactctg	aagtagctgg	tggt				744

<210> 229

<211> 300

<212> DNA

<213> Homo sapien

<400> 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcattgtgaac	60
cattacacat	cgaaataaaa	gaaagggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgc	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggct	ctatttttcc	acctgcagag	gatccagtc	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

<210> 230

<211> 301

<212> DNA

<213> Homo sapien

<400> 230

cagcagaaca	aatacaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcttggttca	cactcaggaa	cgagagctga	cccagtttaag	ggagaagttg	180
cggaaggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301

<210> 231

<211> 301

<212> DNA

<213> Homo sapien

<400> 231

gcaagcacgc	tggcaaatct	ctgtcaggtc	agctccagag	aagccattag	tcatttttagc	60
caggaaactcc	aagtccacat	ccttggcaac	tggggacttg	cgcaggttag	ccttgaggat	120
ggcaacacgg	gactttctcat	caggaaagtgg	gatgtagatg	agctgatcaa	gacggccagg	180
tctgaggatg	gcaggatcaa	tgatgtcagg	ccggttggtg	ccgccaatga	tgaacacatt	240
tttttttgtg	gacatgccat	ccattttctgt	caggatctgg	ttgatgactc	ggtcagcagc	300

301

<400> 232

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<210> 233
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 233

```
<210> 234
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 234

```
<210> 235
<211> 283
<212> DNA
<213> Homo sapien
```

<400> 235

tggggctgtg	cctcaggcgg	gtttgagaaa	tattcaattc	tcagcagaag	ccagaatttg	60
aattccctca	ctcttttaggg	aatcatttac	caggtttgga	gaggattcag	acagctcagg	120
tgctttcact	aatgtctctg	aacttctgtc	cctctttggt	catggatagt	ccaataaata	180
atgttatctt	tgaactgatg	ctcataggag	agaatataag	aactctgagt	gatatcaaca	240

ttagggattc aaagaaatat tagatttaag ctcacactgg tca

283

<210> 236

<211> 301

<212> DNA

<213> Homo sapien

<400> 236

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aggctcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata    60
aatactttta aatcgatcag atttccttaa cccacatgca atcttcttca ccagaagagg    120
tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggatatatag    180
tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta    240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc    300
a                                                    301

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<210> 237

<211> 301

<212> DNA

<213> Homo sapien

<400> 237

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cagtggtagt ggtggtagac gtggcggttg tcgtgggtgcc ttttttggtg cccgtcacaa    60
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg    120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct    180
ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta    240
gggttcogaa attctttctt cctttggata atgtagttca tatccattcc ctcttttato    300
t                                                    301

```

<210> 238

<211> 301

<212> DNA

<213> Homo sapien

<400> 238

```

gggcagggttt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt    60
gttcacagtt cagccccctg ctcagaaaac caacggggcca gctaaggaga ggaggaggca    120
ccttgagact tccggagtcg aggctctcca gggttcccca gcccatcaat cattttctgc    180
acccccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca    240
gtgtgggacc caggggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta    300
t                                                    301

```

<210> 239

<211> 239

<212> DNA

<213> Homo sapien

<400> 239

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ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagttc acataactgc    60
ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa    120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgttttaaaa atagctcaac    180
attcagccag tgagtagagt gtgaatgccg gcatacacag tatacaggtc cttcaggga    239

```

<210> 240
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 240
 ggtcctaattg aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt 60
 gggatctgcc ctccagtgga accttttaag gaagaagtgg gcccaagcta agttccacat 120
 gctgggtgag ccagatgact tctgttccct ggtcactttc ctcaatgggg cgaatggggg 180
 ctgccaggtt tctaaaatca tgcttcatct tgaagcacac ggtcacttca ccttcctcac 240
 gctgtgggtg tactttgatg aaaataccca ctttggtggc ctttctgaag ctataatgtc 300

<210> 241
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 241
 gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga 60
 cctcttttga ggaactcca gcagctatgt tgggtgtctt gagggaatgc aacaaggctg 120
 ctctccatg tattggaaaa ctgcaactg gactcaactg gaaggaaagt ctgctgccag 180
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240
 tctcctcct gtcatacggg ctctctcaag catcctttgt tgtcaggggg ctaaaaggga 300
 g 301

<210> 242
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 242
 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt 60
 tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 120
 gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240
 taagtaccca aagttttata aatcaaaagc cctaataata accattttta gaattcaatc 300
 a 301

<210> 243
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 243
 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60
 ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 120
 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcata tgaccagcgt 180
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccgg 240
 tcaactaccg atgttccaga aaggacagga gacgtccacc aatcccattg ctccattttt 300
 t 301

<210> 244
 <211> 300
 <212> DNA
 <213> Homo sapien

<400> 244
 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa 60
 gtcattgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120
 ccagggaacct tggaaacagt tgacactgta aggtgcttgc tccccaaagac acatcctaaa 180
 aggtgttgta atgggtgaaaa cgtcttcctt ctttattgcc ctttcttatt tatgtgaaca 240
 actgtttgtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatc 300

<210> 245
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 245
 gtctgagtat ttaaaatggt attgaaatta tccccaacca atgttagaaa agaaagaggt 60
 tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120
 aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat 180
 gttttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac 240
 agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa 300
 g 301

<210> 246
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 246
 ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata 60
 acctgggctt attttaaaga actatttgta gtcagattg gttttcctat ggctaaaata 120
 agtgcttctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180
 taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240
 caaatgtgtc ttacaaaaca cgcttcctaac aagggtatgt ttacactacc aatgcagaaa 300
 c 301

<210> 247
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 247
 aggtcctttg gcagggtcct tggatcagag ctcaaactgg agggaaaggc atttcgggta 60
 gcctaagagg gcgactggcg gcagcacaac caaggaaggc aagggtgttt cccccacgct 120
 gtgtcctgtg ttcagggtcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180
 ccttgatgat caagggtggg gcttaagtgg attaaggag gcaagttctg ggttccttgc 240
 cttttcaaac catgaagtca ggctctgtat ccttcctttt cctaactgat attctaacta 300
 a 301

<210> 248
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 248
 aggtccttgg agatgccatt tcagccgaag gactcttctw ttcggaagta caccctcact 60
 attaggaaga ttcttagggg taatttttct gaggaaggag aactagccaa cttagaatt 120
 acaggaagaa agtggtttgg aagacagcca aagaaatzaa agcagattaa attgtatcag 180
 gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag 240
 ctaatgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300
 c 301

<210> 249
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 249
 gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag 60
 ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgcgc 120
 ccaggagagc acagcagtga ctcagagctg gtgcacact gtgcctccct cctcaccgcc 180
 catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240
 actgaatcct tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300
 a 301

<210> 250
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 250
 ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc 60
 cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc 120
 cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac 180
 ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240
 caataaaaacc aaacatgctt ataacattaa gaaaaaceat aaagatacat gattgaaacc 300
 a 301

<210> 251
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 251
 gccgaggtcc tacatttggc ccagtttccc cctgcatact ctccaggggc cctgcctcat 60
 agacaaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat 120
 ggcaggggtc ctcaaaaatg ccaactgtcac tgccaggaaa tgcttctgag cagtacacct 180
 cattggggtc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgga 240
 cctctggagg ggggcagtggt aatcccagct ccaggacgga tcctgtcgaa aagatatcct 300

c

301

<210> 252
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 252
 gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttctca 60
 ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata 120
 tcatttcttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa 180
 atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt 240
 tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300
 a 301

<210> 253
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 253
 ttccctaaga agatgttatt ttgttgggtt ttgttcccc tccatctcga ttctcgtaac 60
 caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccrtagct 120
 tggctctgatt gttttcagac ctraaaatat aaacttgttt cacaagcttt aatccatgtg 180
 gatTTTTTTT cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt 240
 tccatagtgc ccacagggtta ttcctcacat tttctccata ggaaaatgct ttttcccaag 300
 g 301

<210> 254
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 254
 cgctgcgcct ttcccttggg ggagggggcaa ggccagaggg ggtccaagtg cagcacgagg 60
 aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc 120
 ccaaactctt tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa 180
 gaaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc 240
 acttaaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc 300
 t 301

<210> 255
 <211> 302
 <212> DNA
 <213> Homo sapien

<400> 255
 agctTTTTTT tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa 60
 attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat 120
 tgggattttt ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg 180
 aggaaaaagg actggagggtg gaatctttat aaaaaacaag agtgattgag gcagattgta 240

aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac 300
aa 302

<210> 256
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 256
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctccagcct 60
aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc 120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat 180
aggcaaatac ctgctggcaa actggcatta cctggtttgt ggggatggg gggcaagtgt 240
gtggcctctc ggcttggtta gcaagaacat tcagggtatg cctaagttan tcgtgttagt 300
t 301

<210> 257
<211> 301
<212> DNA
<213> Homo sapien

<400> 257
gttgtggagg aactctggct tgctcattaa gtctactga ttttcactat cccctgaatt 60
tccccactta tttttgtctt tcactatcgc aggccttaga agaggtctac ctgcctccag 120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat 180
gtcacattac tcccttcagt gatttcttgt agaagtgcc atccctgaat gccaccaaga 240
tcttaattct cactcttta atcttatctc tttgactcct ctttacaccg gagaaggctc 300
c 301

<210> 258
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 258
cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg 180
atgtctcggt cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat 240
tggtgatccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac 300
t 301

<210> 259
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 259
 tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60
 gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa 120
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt 180
 tccagctcac atctcatctg catgcagcac ggaccgatg cgcccactgg gtcttggtt 240
 cccctccatc ttctcaagca gtgtccttgt tgagccattt gcaccccttg ctccagggtg 300
 c 301

<210> 260
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 260
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt 60
 aaggtgtctt aacttgaaaa agattaggag tcaactggtt acaagttata attgaatgaa 120
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacia caggattaac 180
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttataaaac agactgatc 240
 actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca 300
 c 301

<210> 261
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 261
 aaatattcga gcaaatcctg taactaatgt gtctcrataa aaggctttga actcagtga 60
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120
 agcaccaact attccatata attcatcagc aggaaataaa ggctcttcag aaggttcaat 180
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcttag ttaagtgaag 240
 ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300
 a 301

<210> 262
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 262

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gaggagagcc tgttacagca ttgtgaagca cagaatactc caggagtatt tgtaattgtc      60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc      120
cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca ttgtaatga      180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcc      240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat      300
c                                                                    301

```

```

<210> 263
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 263
tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg      60
aaaattacta cttaactcta attcacaata acaatggcat taaggtttga cttgagttgg      120
ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat      180
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg      240
agatgctaag gcccacagaga tcgtttgatc caacctctct atcttcagag gggaaaatgg      300
g                                                                    301

```

```

<210> 264
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 264
aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc      60
aatgaatgac tctaaaaaca atattttacat ttaatggttt gtagacaata aaaaaacaag      120
gtggatagat ctagaattgt aacattttta gaaaaccata scatrtgaca gatgagaaag      180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac      240
acccttcata taaattcact atcttggett gaggcactcc ataaaatgta tcacgtgcat      300
a                                                                    301

```

```

<210> 265
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 265
tgcccaagtt atgtgtgaagt gtatccgcac ccagaggtaa aactacactg tcctctttgt      60
cttcttgtga cgagtatatt cttctctggg gagaagccgg gaagtcttct cctggctcta      120
catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggagggga      180
ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag      240
cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg      300
c                                                                    301

```

<210> 266

<211> 301

<212> DNA

<213> Homo sapien

<400> 266

taccgtctgc	ccttcctccc	atccaggcca	tctgogaatc	tacatgggtc	ctcctattcg	60
acaccagatc	actctttcct	ctacccacag	gcttgctatg	agcaagagac	acaacctcct	120
ctcttctgtg	ttccagcttc	ttttcctggt	cttcccaccc	cttaagttct	attcctgggg	180
atagagacac	caatacccat	aacctctctc	ctaagcctcc	ttataaccca	gggtgcacag	240
cacagactcc	tgacaactgg	taaggccaat	gaactgggag	ctcacagctg	gctgtgcctg	300
a						301

<210> 267

<211> 301

<212> DNA

<213> Homo sapien

<400> 267

aaagagcaca	ggccagctca	gcctgcoctg	gccatctaga	ctcagcctgg	ctccatgggg	60
gttctcagtg	ctgagtcctat	ccaggaaaag	ctcacctaga	ccttctgagg	ctgaatcttc	120
atcctcacag	gcagcttctg	agagcctgat	attcctagcc	ttgatgggtc	ggagtaaagc	180
ctcattctga	ttcctctcct	tcttttcttt	caagttggct	ttcctcacat	ccctctgttc	240
aattcgcttc	agcttgtctg	ctttagccct	catttccaga	agcttcttct	ctttggcctc	300
t						301

<210> 268

<211> 301

<212> DNA

<213> Homo sapien

<400> 268

aatgtctcac	tcaactactt	cccagcctac	cgtggcctaa	ttctgggagt	tttcttctta	60
gatcttggga	gagctgggtc	ttctaaggag	aaggaggaag	gacagatgta	acttrggatc	120
tcgaagagga	agtctaattg	aagtaattag	tcaacgggtc	ttgttttagac	tcttgggaata	180
tgctgggtgg	ctcagtgagc	ccttttggag	aaagcaagta	ttattcttaa	ggagtaacca	240
cttcccattg	ttctactttc	taccatcctc	aattgtatat	tatgtattct	ttggagaact	300
a						301

<210> 269

<211> 301

<212> DNA

<213> Homo sapien

<400> 269

taacaatata	cactagctat	ctttttaact	gtccatcatt	agcaccaatg	aagattcaat	60
aaaattacct	ttattcacac	atctcaaaac	aattctgcaa	attcttagtg	aagtttaact	120
atagtcacag	accttaata	ttcacattgt	tttctatgtc	tactgaaaat	aagttcacta	180
cttttctgga	tattctttac	aaaatcttat	taaaattcct	ggattatca	cccccaatta	240
tacagtagca	caaccacctt	atgtagtttt	tacatgatag	ctctgtagaa	gtttcacatc	300
t						301

<210> 270
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 270
 cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60
 cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcæa 180
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300
 a 301

<210> 271
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 271
 aaaaggttct cataagatta acaattttaa taaatatttg atagaacatt ctttctcatt 60
 tttatagctc atcttttaggg ttgatattca gttcatgcctt cctttgctgc tcttgatcca 120
 gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt ggggtccaagg 180
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240
 tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300
 c 301

<210> 272
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 272
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
 tccaataatt cctcatgat gagcaagaaa aattctttgc gcacccctcc tgcacccaca 180
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240
 ctaaggactt ccattgcac tctacaata ttttctctac gcaccactag aattaagcag 300
 g 301

<210> 273
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>

seq#1112360111

<221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 273
 acatgtgtgt atgtgtatct ttgggaaaaan aanaagacat cttgtttayt attttttttg 60
 agagangctg ggacatggat aatcacwtaa ttgtctayta tyactttaat ctgactygaa 120
 gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc 180
 ttytttctgt ccagagagag tatcagtgc ananatttma gggagaamac atgmattggg 240
 gggacttnty tttaacngam accctgcccg sgccgcccctg makcngantt ccgcsananc 300
 t 301

<210> 274
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 274
 cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg 60
 aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa 120
 tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca 180
 tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc 240
 aattgtgctt cttttgataa gaagctttct tggatcatatc aggaaattcc aganaaaagt 300
 c 301

<210> 275
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 275
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 gggtgaaatt ggccaacttt ctattaactt atgttggaat ttttgccacc aacagtaagg 120
 tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag 180
 tcaagagact ccagggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc 240
 agatatccat cacactggcg gncgctcgan catgcactta gaaggnccaa ttcgccctat 300
 a 301

<210> 276
 <211> 301
 <212> DNA

<213> Homo sapien

<400> 276

tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat	60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat	120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc	180
caatacatitt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt	240
aaaactattc agtatgtttc ctttgcttca tgtctgagaa ggctctcctt caatggggat	300
g	301

<210> 277

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 277

tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag	60
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacatcg	120
gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccga cctcgtcct	180
caccatagtg gggagactaa agtggccacg gatttgctt anggtgtgcag tgcgttctga	240
gttcnctgtc gattacatct gaccagtctc ctttttccga agtcctccg ttcaatcttg	300
c	301

<210> 278

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 278

taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat	60
aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca	120
cagtctctac tgttattatg cattacctgg gaatttataat aagcccttaa taataatgcc	180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacaggttt	240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt	300
c	301

<210> 279

<211> 301

<212> DNA

<213> Homo sapien

tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag

<400>	282						
cagggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca		60
tccagaaccc	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga		120
agcgcagaag	caaagcccg	gcagaaccat	gctaacctta	cagctcagcc	tgcacagaag		180
cgcagaagca	aagcccgagc	agaaccatgc	taaccttaca	gctcagcctg	cacagaagcg		240
cagaagcaaa	gcccgaggcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag		300
a							301

<210> 283
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 283
 atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag 60
 cactttgagg gctttataat aatatgctgc ttgaaaaaa aaatgtgtag ttgatactca 120
 gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc 180
 acttcccagg ttttatgcaa aaattttggt aaattctata atggtgatat gcactcttta 240
 ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt 300
 g 301

<210> 284
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 284
 caggtaaaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt 60
 gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa 120
 gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcac 180
 ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240
 actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt 300
 a 301

<210> 285
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 285
 acatcaccat gatcggatcc cccacccatt atacgctgta tgtttacata aatactcttc 60
 aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
 caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
 attaaatatg tctgacttct tttgaggtca cagcactagg caaatgctat ttacgatctg 240
 caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag 300
 t 301

<210> 286
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 286

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<210> 287
<211> 301
<212> DNA
<213> Homo sapien
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<210> 288
<211> 301
<212> DNA
<213> Homo sapien
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<210> 289
<211> 301
<212> DNA
<213> Homo sapien
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<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
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<400>	289						
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gcttttgatg	tctccaagta	gtccaccttc	atttaactct	ttgaaactgt	atcatctttg		120
ccaagtaaga	gtggtggcct	atttcagctg	ctttgacaaa	atgactggct	cctgacttaa		180
cgttctataa	atgaatgtgc	tgaagcaaag	tgcccatggt	ggcggcggaan	aagagaaaga		240
tgtgttttgt	tttgactct	ctgtggtccc	ttccaatgct	gtgggtttcc	aaccagnnga		300
a							301

<210> 290
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 290
 acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60
 tgactgatct gttcatttct ctacacagctc ttaccccca aagcttttcc accctaagtg 120
 ttctgacctc tttttcta at cacagtaggg atagaggcag anccacctac aatgaacatg 180
 gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc 240
 tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgcg 300
 a 301

<210> 291
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 291
 caggtaccaa tttcttctat cctagaaaca tttcatttta tgttggtgaa acataacaac 60
 tatatagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120
 tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180
 agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa 240
 acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct 300
 a 301

<210> 292
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 292
 accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60
 tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180
 ggaaatatag tasttyatga atgttnatta aattccagtc ataatagtgg ctacacactc 240
 tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa 300
 a 301

<210> 293
 <211> 301

<212> DNA

<213> Homo sapien

<400> 293

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ggtaccaagt gctggtgcca gcctggtacc tgttctcact gaaaagtctg gctaattgctc    60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt    120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt    180
gtgagaatth tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg    240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcagagcat    300
g                                                                    301

```

<210> 294

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 294

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tgaccataaa caatatacac tagctatctt tttactgtc catcattagc accaatgaag    60
attcaataaaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag    120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag    180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc    240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt    300
t                                                                    301

```

<210> 295

<211> 305

<212> DNA

<213> Homo sapien

<400> 295

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gtactctttc tctccctccc tctgaattta attctttcaa cttgcaattt gcaaggatta    60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac    120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga    180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacagggtga attggatggt    240
tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt    300
tctct                                                                    305

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<210> 296

<211> 301

<212> DNA

<213> Homo sapien

<400> 296

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aggtagctatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct    60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg    120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac    180

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tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt 240
 tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg 300
 c 301

<210> 297
 <211> 300
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(300)
 <223> n = A,T,C or G

<400> 297
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 aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga 120
 acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt 180
 tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc 240
 accgcacctc ggcgcgcacc acgctaagcc gaattctgca gatatccatc acactggcgg 300

<210> 298
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 298
 tatgggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc cctcccgcg 60
 ggcattctgag agacctggtg ttccagtgtt tctggaaatg ggteccagtg ccgccggctg 120
 tgaagctctc agatcaatca cgggaagggc ctggcggttg tggccacctg gaaccaccct 180
 gtccctgtctg ttacatttcc actaycaggt tttctctggg cattacnatt tgttccccta 240
 caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcagggtggc ctcagcgagg 300
 t 301

<210> 299
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 299
 gttttgagac ggagttttcac tcttggtgcc cagactggac tgcaatggca gggctctctgc 60
 tcaactgcacc ctctgcctcc cagggttcgag caattctcct gctcagcct cccaggtagc 120
 tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180
 gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct 240
 cggcctccca aagtgtctgga attataggca tgagtcaaca cggccagcct aaagatatatt 300
 t 301

<210> 300
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 300
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 gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta 180
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgcccacc gtcttggtac 240
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccagagc catcccccat 300
 g 301

<210> 301
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 301
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 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120
 gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaaagacc 180
 ctgagagctg agacaccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300
 t 301

<210> 302
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 302
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 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120
 ttgagttggt tcttagtatt atttatggta aataggtctt taccacttgc aaataactgg 180
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240
 caggatttga gatgctaagg ccccagagat cgtttgatcc aacctctta ttttcagagg 300
 g 301

<210> 303
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 303
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 tggtaaatgg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300

C

301

<210> 304
 <211> 301
 <212> DNA
 <213> Homo sapien

<400> 304
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 tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120
 ctttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctgggtgcagt 180
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240
 ttttcctttt gtaatcaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300
 C 301

<210> 305
 <211> 301
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(301)
 <223> n = A,T,C or G

<400> 305
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 cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120
 taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag 180
 aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa 240
 ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300
 a 301

<210> 306
 <211> 8
 <212> PRT
 <213> Homo sapien

<400> 306
 Val Leu Gly Trp Val Ala Glu Leu
 1 5

<210> 307
 <211> 637
 <212> DNA
 <213> Homo sapien

<400> 307
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 ttgtgatcag gtgggtctatg gggtttatcc ctacaaagaa gaatccagaa ataggggcac 120
 attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180

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cacaccattg	gtgagggagg	gattaccacc	ctgggggttat	gaagatgggtt	gaacacccca	240
cacatagcac	cggagatatg	agatcaacag	tttcttagcc	atagagattc	acagcccaga	300
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<210> 308

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 308

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ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
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ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
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catttttgtg	gtggataaag	tcaggatgcc	caggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gccatgaaga	cttgagggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggcaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
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<210> 309

<211> 460

<212> DNA

<213> Homo sapien

<400> 309

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gagcacatct	tcagcaagag	ggggaaatac	tcatcatttt	tggccagcag	ttgtttgatc	180
accaaaccatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtccg	240
ggggaattta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctaccag	300
ctgggggtgt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggtaacc	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

<210> 310

<211> 539

<212> DNA

<213> Homo sapien

<400> 310

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acgggactta tcaataaaag ataggaaaag aagaaaactc aaatattata ggcagaaatg      60
ctaaagggtt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt      120
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa      180
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatgggtatg attttagcaa      240
taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa      300
ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac      360
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc aactgtgac      420
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc      480
atattttcac cccacaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga      539

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<210> 311

<211> 526

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(526)

<223> n = A,T,C or G

<400> 311

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caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc      60
ttttgacggt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta      120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa      180
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg      240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa      300
aaaattgggga aactctgaag ggttttaagt atcttacctg aagctaraga ctccataaacc      360
tctctttaca gggagctcct gcagcccta cagaaatgag tggctgagat tcttgattgc      420
acagcaagag cttctcatct aaacccttcc cttttttagt atctgtgtat caagtataaa      480
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<210> 312

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(500)

<223> n = A,T,C or G

<400> 312

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cctctctctc cccacccctt gactctagag aactgggttt tctcccagta ctccagcaat      60
tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct      120
ccattttctc ttcccttcca cctgccagtt ttgctgactc tcaacttgct atgagtgtaa      180
gcattaagga cattatgctt cttcgattct gaagacagggc cctgctcatg gatgactctg      240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atccctctct      300
tgcagatgtc tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct      360
tgctaattgt gtttcctttg taaaccanga ttcttatttg nctgggtatg aatatcagct      420

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ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt 480
tagtcttaat tatctattgg 500

<210> 313
<211> 718
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(718)
<223> n = A,T,C or G

<400> 313
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tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat 120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa 180
gtagtacat gtttttgac atttccagcc ctttttaaata tccacacaca caggaagcac 240
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga 300
gcctcgccct gtgcctgntc ccgcttgtga ggggaaggaca ttagaaaaatg aattgatgtg 360
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aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg 600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaataac tgacttacgg 660
ttcttntggc ccacattttc atnateccac centcntttt aannttantic caaantgt 718

<210> 314
<211> 358
<212> DNA
<213> Homo sapien

<400> 314
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caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtatg tgtagtccaa 180
gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc 240
ttgttgtatt gctgaactgt agtgccctgt attttgcctc tgtctgtgaa ttctgttgct 300
tctggggcat ttoccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315
<211> 341
<212> DNA
<213> Homo sapien

<400> 315
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gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180
agtcaccagc tccccgacca gccggatata gtccttaggg gtcattgtag cttcctgaag 240
tagcttctgc tgtaagaggg tgttgtcccg ggggctcgtg cggttattgg tctgggctt 300

gagggggcgg tagatgcagc acatggtgaa gcagatgatg t 341

<210> 316

<211> 151

<212> DNA

<213> Homo sapien

<400> 316

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tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120
cattcaggga gctctgggtg caatattagt t 151

<210> 317

<211> 151

<212> DNA

<213> Homo sapien

<400> 317

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atcttcattt atctctggcc ttaacctggc ctccctgagge tgccggccagc agatcccagg 120
ccagggtctt gttcttgcca cactgcttg a 151

<210> 318

<211> 151

<212> DNA

<213> Homo sapien

<400> 318

actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcggg gggacctcct 60
gctgcaggct ggagtgctctt tattcctggc gggagaccgc acattccact gctgaggctg 120
tgggggcggg ttatcaggca gtgataaaca t 151

<210> 319

<211> 151

<212> DNA

<213> Homo sapien

<400> 319

aactagtggg tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta 60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg 120
taagattggg tttatgtgat tttagtgggt a 151

<210> 320

<211> 150

<212> DNA

<213> Homo sapien

<400> 320

aactagtggg tccactagtc cagtgtgggt gaattccatt gtgttggggg tctagatcgc 60
gagcggctgc cctttttttt tttttttttt ggggggaatt tttttttttt aatagttatt 120
gagtgttcta cagcttacag taaataccat 150

<210> 321
 <211> 151
 <212> DNA
 <213> Homo sapien

<400> 321
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 taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120
 tgcctctgag aaatcaaagt cttcatacac t 151

<210> 322
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 322
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 tttgggcttg gtcagtttgc cacagggctt ggagatgggtg acagtcttct ggcattcggc 120
 attgtgcagg gctcgttca nacttcagtt t 151

<210> 323
 <211> 151
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(151)
 <223> n = A,T,C or G

<400> 323
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 nagactcant tactaccag tttgtgggtt twtgggagaa atgtaactgg acagtttagct 120
 gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324
 <211> 461
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(461)
 <223> n = A,T,C or G

<400> 324
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 agaagtgggc agctaaagga atccagggtg ttgggttgac tgtaataacc tttgatgaaa 120
 agagttacta cgaatcccat cttgggtcca gctatatcac tgacagcatg gtagaagact 180
 gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc 240
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 cacacaaatg caatagttgg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt 360
 gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga 420
 aaaaacgcac aagagccctt gccctgccct agctgangca c 461

<210> 325

<211> 400

<212> DNA

<213> Homo sapien

<400> 325
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 agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt 180
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 gtcccttttg cattgccaaag tgccataacc atgagcacta cgctaccatg gttctgcctc 360
 ctggccaagc aggctgggtt gcaagaatga aatgaatgat 400

<210> 326

<211> 1215

<212> DNA

<213> Homo sapien

<400> 326
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<210> 327
 <211> 220
 <212> PRT
 <213> Homo sapien

<400> 327
 Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
 1 5 10 15
 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
 20 25 30
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
 35 40 45
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
 50 55 60
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
 65 70 75 80
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
 85 90 95
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
 100 105 110
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
 115 120 125
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
 130 135 140
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
 145 150 155 160
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
 165 170 175
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
 180 185 190
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
 195 200 205
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 210 215 220

<210> 328
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 328
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 atccgcagtg ggtgctgtca gccacacact gtttccagaa ctctacacc atcgggctgg 180
 gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gccca 234

<210> 329
 <211> 77
 <212> PRT
 <213> Homo sapien

<400> 329
 Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
 1 5 10 15
 Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
 20 25 30
 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
 35 40 45
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
 50 55 60
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
 65 70 75

<210> 330

<211> 70

<212> DNA

<213> Homo sapien

<400> 330
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 gctgcagcca 70

<210> 331

<211> 22

<212> PRT

<213> Homo sapien

<400> 331
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
 1 5 10 15
 Val Ser Gly Ser Cys Ser
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<210> 332

<211> 2507

<212> DNA

<213> Homo sapien

<400> 332
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 gtacatcaac tggtcagctt cctgggaaaag tagttgtggt cacaggagct aatacaggta 180
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<210> 333

<211> 3030

<212> DNA

<213> Homo sapien

<400> 333

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<211> 2417

<212> DNA

<213> Homo sapien

<400> 334

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<211> 2984

<212> DNA

<213> Homo sapien

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<210> 336

<211> 147

<212> PRT

<213> Homo sapien

<400> 336

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			20					25				30			

Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
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 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
 50 55 60
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
 65 70 75 80
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
 85 90 95
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
 100 105 110
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 Ala Phe Trp
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<210> 337
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 <212> PRT
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<210> 338
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 <211> 318
 <212> PRT
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 Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly
 35 40 45
 Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
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 Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu

65 70 75 80
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 85 90 95
 Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
 100 105 110
 Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
 115 120 125
 Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met
 130 135 140
 His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu
 145 150 155 160
 Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser
 165 170 175
 Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
 180 185 190
 Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
 195 200 205
 Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly
 210 215 220
 Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val
 225 230 235 240
 Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe
 245 250 255
 Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu
 260 265 270
 Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His
 275 280 285
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<210> 340

<211> 483

<212> DNA

<213> Homo sapien

<400> 340

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<210> 341

<211> 344

<212> DNA

<213> Homo sapien

<400> 341

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<211> 592

<212> DNA

<213> Homo sapien

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<210> 343

<211> 382

<212> DNA

<213> Homo sapien

<400> 343

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<210> 344

<211> 536

<212> DNA

<213> Homo sapien

<400> 344

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<210> 345

<211> 251

<212> DNA

<213> Homo sapien

<400> 345

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<212> DNA

<213> Homo sapien

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<221> misc_feature

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<223> n = A,T,C or G

<400> 346

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<210> 347

<211> 201

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

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<223> n = A,T,C or G

<400> 347

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<210> 348
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 348
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<210> 349
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 349
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<210> 350
 <211> 908
 <212> DNA
 <213> Homo sapien

<400> 350
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 ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt 600
 catgtctttg ggtcgatgtc aagataaac aactacaact actaagtctg aagatgggca 660
 ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca 720
 ccacatacct tgtccggaac attacaatgg cttctgcatt catgggaagt gtgagcattc 780
 tatcaatatg caggagccat cttgcagggt tgatgctggt tatactggac aacactgtga 840
 aaaaaaggac tacagtgttc tatacgttgt tcccggctct gtacgatttc agtatgtctt 900
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<210> 351
 <211> 472
 <212> DNA
 <213> Homo sapien

<400> 351

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gtcaaacc	ttt	aatgccattg	tt	tattgtgaa	ttaggattaa	gtagtaattt	tcaaaattca	120
cattaact	ttg	at	ttt	taaaat	cagwtttgyg	agtcatttac	cacaagctaa	180
tatgataaaa	aca	accattg	tatt	cctggt	tttctaaaca	gtcctaattt	ctaactgt	240
atatatcctt	cg	acatcaat	ga	actttgtt	ttcttttact	ccagtaataa	agtaggcaca	300
gatctgtcca	ca	acaaaactt	gccc	tctcat	gccttgctc	tcaccatget	ctgctccagg	360
tcagccccct	ttt	ggcctgt	tt	gttttgtc	aaaaacctaa	tctgcttctt	gcttttcttg	420
gtaatatata	tt	tagggaag	at	gttgcttt	gcccacacac	gaagcaaagt	aa	472

<210> 352

<211> 251

<212> DNA

<213> Homo sapien

<400> 352

ctcaaagcta	at	ctctcggg	aat	caaacca	gaaaagggca	aggatcttag	gcatgggtgga	60
tgtggataag	gcc	aggtcaa	tg	gctgcaag	catgcagaga	aagaggtaca	tgggagcgtg	120
caggctgcgt	tcc	gtcctta	cg	atgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
atacatggaa	agg	agggggga	ag	ccaaccca	gaaatgggct	ttctctaate	ctgggatacc	240
aataagcaca	a							251

<210> 353

<211> 436

<212> DNA

<213> Homo sapien

<400> 353

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cacattatgg	tattattact	atactgatta	tatt	tatcat	gtgacttcta	attaraaaat		120
gtatccaaaa	gcaaaacagc	agatatacaa	aatt	aaagag	acagaagata	gacattaaca		180
gataaggcaa	cttatacatt	gacaatccaa	at	ccaataca	tttaaacatt	tgggaaatga		240
gggggacaaa	tggaagccar	atcaaatttg	tg	taaaaacta	ttcagtatgt	ttcccttgct		300
tcatgtctga	raaggtcttc	ccttcaatgg	gg	atgacaaa	ctccaaatgc	cacacaaatg		360
ttaacagaat	actagattca	caactggaacg	gg	ggtaaaaga	agaaattatt	ttctataaaa		420
gggctcctaa	tgtagt							436

<210> 354

<211> 854

<212> DNA

<213> Homo sapien

<400> 354

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caagtctgaa	ac	caaatacta	gg	aaacatag	gaaacgagcc	aggcacaggg	ctggtggggc		120
atcagggaacc	acc	ctttggg	tt	gatatttt	gcttaatctg	catcttttga	gtaagatcat		180
ctggcagtag	aa	gtgttct	cc	aggtacat	ttctctagct	catgtacaaa	aacatcctga		240
aggactttgt	cagg	tgccctt	gct	aaaagcc	agatgcgttc	ggcacttcct	tggtctgagg		300
ttaattgcac	acct	acaggc	act	gggctca	tgctttcaag	tattttgtcc	tcacttttagg		360
gtgagtgaaa	gat	ccccatt	at	aggagcac	ttgggagaga	tcatataaaa	gctgactctt		420

gagtacatgc	agtaatgggg	tagatgtgtg	tgggtgtgtct	tcattcctgc	aaggggtgctt	480
gttagggagt	gtttccagga	ggaacaagtc	tgaaaccaat	catgaaataa	atggtaggtg	540
tgaactggaa	aactaattca	aaagagagat	cgtgatatca	gtgtggttga	tacaccttgg	600
caatatggaa	ggctctaatt	tgcccatatt	tgaaataata	attcagcttt	ttgtaataca	660
aaataacaaa	ggattgagaa	tcatgggtgc	taatgtataa	aagacccagg	aaacataaat	720
atatcaactg	cataaatgta	aaatgcatgt	gacccaagaa	ggccccaag	tggcagacaa	780
cattgtaccc	attttccctt	ccaaaatgtg	agcggcgggc	ctgctgcttt	caaggctgtc	840
acacgggatg	tcag					854

<210> 355

<211> 676

<212> DNA

<213> Homo sapien

<400> 355

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caggtcaaag	ctgatctttc	tggaatgtca	ccaaccaagg	gcctatattt	atcaaaagcc	120
atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaag	cctaccaatg	agagctcagt	tcaaggcgaa	ccaccccttc	240
ctgttcttta	taaggcacac	tcataccaac	acgatcctat	tctgtggcaa	gcttgcctct	300
ccctaatacg	atgggggtga	gtaaggctca	gagttgcaga	tgaggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aagctgttca	cacctcacgc	acctctgtgc	ctcagtttgc	420
tcactgtcaa	aatagggtcta	ggatttcttc	caacctattc	atgagttgtg	aagctaaggc	480
tttgttaatc	atggaaaaag	gtagacttat	gcagaaagcc	tttctggctt	tcttatctgt	540
ggtgtctcat	ttgagtgtcg	tccagtgaca	tgatcaagtc	aatgagtaaa	attttaaggg	600
attagatttt	cttgacttgt	atgtatctgt	gagatcttga	ataagtgacc	tgacatctct	660
gcttaaagaa	aaccag					676

<210> 356

<211> 574

<212> DNA

<213> Homo sapien

<400> 356

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catgtggcac	ctgactggca	tcaaaccaaa	gttcgtaggc	caacaaagat	gggccactca	120
caagcttccc	atttgtagat	ctcagtgcc	atgagtatct	gacacctgtt	cctctcttca	180
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aaaagtccac	aaaactgcag	tctttgctgg	gatagtaagc	caagcagtcg	ctggacagca	300
gagttctttt	cttgggcaac	agataaccag	acaggactct	aatcgtgctc	ttattcaaca	360
ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acaggggaagg	420
agatacaagc	tcgtttacat	gtgatagatc	taacaaaggc	atctaccgaa	gtctggctcg	480
gatagacggc	acagggagct	cttaggtcag	cgctgctggg	tggaggacat	tcctgagtc	540
agctttgcag	cctttgtgca	acagtacttt	ccca			574

<210> 357

<211> 393

<212> DNA

<213> Homo sapien

<400> 357

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taatatggkg	kcttggtcac	tatacttaaa	aatgcaccac	tcataaatat	ttaattcagc	120
aagccacaac	caaracttga	ttttatcaac	aaaaaccct	aaatataaac	ggsaaaaaag	180
atagatatata	ttattccagt	ttttttaaaa	cgtaaaaarat	attccattgc	cgaattaara	240
araarataag	tgtttatatg	aaagaagggc	attcaagcac	actaaaraaa	cct.gaggkaa	300
gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
tttttttctt	tttctgtttt	tttttttttt	tac			393

<210> 358

<211> 630

<212> DNA

<213> Homo sapien

<400> 358

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ttaatgttta	taggaaaatg	atgagtttat	gacaaaggaa	gtagatagtg	ttttacaaga	120
gcatagagta	gggaagctaa	tccagcacag	ggaggtcaca	gagacatccc	taaggaagtg	180
gagtttaaac	tgagagaagc	aagtgcctta	actgaaggat	gtgttgaaga	agaagggaga	240
gtagaacaat	ttgggcagag	ggaaccttat	agaccttaag	gtgggaaggt	tcaaagaact	300
gaaagagagc	tagaacagct	ggagccgttc	tccgggtgta	agaggagtca	aagagataag	360
attaaagatg	tgaagattaa	gatcttggtg	gcattcaggg	attggcactt	ctacaagaaa	420
tactgaagg	gagtaatgtg	acattacttt	tcacttcagg	atggccattc	taactccagg	480
gggtagactg	gactaggtaa	gacrggaggc	aggtagacct	cttctaaggc	ctgcatagtg	540
gaaagacaaa	aataagcggg	gaaattcagg	ggatagtga	aaccagtagg	acttaatgag	600
caagccagag	gttcctccac	aacaaccagt				630

<210> 359

<211> 620

<212> DNA

<213> Homo sapien

<400> 359

acagcattcc	aaaatataca	tctagagact	aarrgtaaat	gctctatagt	gaagaagtaa	60
taattaaaaa	atgctactaa	tatagaaaat	ttataatcag	aaaaataaat	attcagggag	120
ctcaccagaa	gaataaagtg	ctctgccagt	tattaaagga	ttactgctgg	tgaattaaat	180
atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240
aggattaact	gttttaggaa	cagatataaa	gcttcgccac	ggaagagatg	gacaaagcac	300
aaagacaaca	tgatacctta	ggaagcaaca	ctaccttttc	aggcataaaa	tttgagaaaa	360
tgcaacatta	tgcttcatga	ataatatgta	gaaagaaggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcataatacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacaccaaa	caaaaccatc	aacttatatt	gtattctata	acatacgaga	600
ctgtaaagat	gtgacagtgt					620

<210> 360

<211> 431

<212> DNA

<213> Homo sapien

<400> 360

aaaaaaaaaa	agccagaaca	acatgtgata	gataatatga	ttggctgcac	acttccagac	60
------------	------------	------------	------------	------------	------------	----

tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa	120
tactcatcat ttttggccag cagttgtttg atcaccaaac atcatgccag aatactcagc	180
aaaccttctt agctcttgag aagtcaaagt ccgggggaat ttattcctgg caattttaat	240
tggactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgctact	300
agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg	360
tgatgccaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcggtgtgt	420
agattcttag t	431

<210> 361

<211> 351

<212> DNA

<213> Homo sapien

<400> 361

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ttgggtctct tgggtctcttg .ccaagtttcc cagccactcg agggagaaat atcggggagg	180
ttgacttcct ccggggcttt cccgagggct tcaccgtgag ccctgcggcc ctgagggtg	240
caatcctgga ttcaatgtct gaaacctcgc .tctctgcctg ctggacttct gagggcgtca	300
ctgccactct gtctctccagc tctgacagct cctcatctgt ggtcctgttg t	351

<210> 362

<211> 463

<212> DNA

<213> Homo sapien

<400> 362

acttcatcag gccataatgg gtgcctcccg tgagaatcca agcacctttg gactgcgcga	60
tgtagatgag ccggctgaag atcttgcgca tgcgcggctt cagggcgaag ttcttggcgc	120
ccccggtcac agaaatgacc aggttgggtg ttttcagggt ccagtgtctg gtcagcagct	180
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttcctt ttcttcccca	240
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttcttgggtg tgtttcttgt	300
agttccattt ctcaactttg ttgatctggg tgcttccat gtgctggctc tgggcatagc	360
cacacttgca cacattctcc ctgataagca cgatgggtgt gacaggaagg aaggatttca	420
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<210> 363

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 363

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tgggaggcac tacgcaagat gggactgcgt cctgggggtga gacatcctct ccttggagat	180
ctaacgaaac ttctcaccta tgagttgtaa agcagaaata cctgnactac agacgagtgc	240

ccaacagcaa	ccccccggaa	gtatgagttc	ctctrgggcc	tccgttccta	ccatgagasc	300
tagcaagatg	naagtgttga	gantcattgc	agagggttcag	aaaagagacc	cntcgtgact	360
ggtctgcaca	gttcatggag	gctgcagatg	aggccttggg	tgctctggat	gctgctgcag	420
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ntgggccctg	gagctgggat	gacattgagt	ttgagctgct	gacctgggat	gaggaaggag	540
attttggaga	tccntgggtc	agaattccat	ttaccttctg	ggccagatac	caccagaatg	600
cccgtccag	attccctcag	acctttgccc	gtcccattat	tggtcstggg	ggt	653

<210> 364

<211> 401

<212> DNA

<213> Homo sapien

<400> 364

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aaaacaaggt	ggatagatct	agaattgtaa	cattttaaaga	aaaccatagc	atttgacaga	180
tgagaaagct	caattataga	tgcaaagtta	taactaaact	actatagtag	taaagaaata	240
catttcacac	ccttcataata	aattcactat	cttggttga	ggcactccat	aaaatgtatc	300
acgtgcatag	taaatcttta	tatttgctat	ggcgttgac	tagaggactt	ggactgcaac	360
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<210> 365

<211> 356

<212> DNA

<213> Homo sapien

<400> 365

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taccagagca	tcaagtctct	gcagcaggtc	attcttgggt	aaagaaatga	cttccacaaa	180
ctctccatcc	cctgggctttg	gcttcggcct	tgcgttttcg	gcacatcttc	cgttaatggg	240
gactgtcacg	atgtgtatag	tacagtttga	caagcctggg	tccatacaga	ccgctggaga	300
acattcggca	atgtccctt	tgtagccagt	ttcttcttcg	agctcccggg	gagcag	356

<210> 366

<211> 1851

<212> DNA

<213> Homo sapien

<400> 366

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tcacttcctt	taagcctttg	tgactcttcc	tctgatgtca	gctttaagtc	ttgttctgga	180
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caaattacat	gatgatgact	agaaacagca	tactctctgg	ccgtctttcc	agatcttgag	300
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cagcaagtat	gagagcagtt	cttccatata	tatccagcgc	atttaaattc	gcttttttct	420
tgattaaaaa	tttcaccact	tgctgttttt	gctcatgtat	accaagtagc	agtgggtgtga	480
ggccatgctt	gttttttgat	tccatatacag	caccgtataa	gagcagtgct	ttggccatta	540
atztatcttc	attgtagaca	gcatagtgta	gagtgggtatt	tccataactca	tctggaatat	600

ttggatcagt	gccatgttcc	agcaacatta	acgcacattc	atcttcctgg	cattgtacgg	660
cctttgtcag	agctgtcctc	tttttgttgt	caaggacatt	aagttgacat	cgtctgtcca	720
gcacgagttt	tactacttct	gaattcccat	tggcagaggc	cagatgtaga	gcagtcctct	780
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gctcctgaga	aacaccccag	ctcttccggg	ctaacacagg	caagtcaata	aatgtgataa	1620
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tttgacaaaa	tccagcatcc	ttgtatttat	tgttgcagtt	ctcagaggaa	atgctttctaa	1740
cttttcccca	tttagtatta	tgttggctgt	gggcttgtca	taggtggttt	ttattacttt	1800
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<210> 367

<211> 668

<212> DNA

<213> Homo sapien

<400> 367

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accrtataag	agcagtgtct	tggccattaa	tttatctttc	atrrtagaca	gcrtagtgya	180
gagtgggtatt	tcataactca	tctggaatat	ttggatcagt	gccatgttcc	agcaacatta	240
acgcacattc	atcttcctgg	cattgtacgg	cctgtcagta	ttagacccaa	aaacaaatta	300
catactcttag	gaattcaaaa	taacattcca	cagctttcac	caactagtta	tattttaagg	360
agaaaactca	tttttatgcc	atgtattgaa	atcaaaccce	cctcatgctg	atatagttgg	420
ctactgcata	cctttatcag	agctgtcctc	tttttgttgt	caaggacatt	aagttgacat	480
cgtctgtcca	gcaggagttt	tactacttct	gaattcccat	tggcagaggc	cagatgtaga	540
gcagtcctat	gagagtgaga	agacttttta	ggaaattgta	gtgcactagc	tacagccata	600
gcaatgattc	atgtaactgc	aaacactgaa	tagcctgcta	ttactctgcc	ttcaaaaaaa	660
aaaaaaaa						668

<210> 368

<211> 1512.

<212> DNA

<213> Homo sapien

<400> 368

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ttcaaacaga	ttggaaaccc	ggagttacct	gctagtgggt	gaaactgggt	ggtagacgcg	180
atctgttggc	tactactggc	ttctcctggc	tgttaaaagc	agatgggtgg	tgaggttgat	240

tccatgccgg	ctgcttcttc	tgtgaagaag	ccatttggtc	tcaggagcaa	gatgggcaag	300
tggtgctgcc	gttgcttccc	ctgctgcagg	gagagcggca	agagcaacgt	gggcacttct	360
ggagaccacg	acgactctgc	tatgaagaca	ctcaggagca	agatgggcaa	gtggtgccgc	420
cactgcttcc	cctgctgcag	ggggagtggc	aagagcaacg	tgggcgcttc	tggagaccac	480
gacgaytctg	ctatgaagac	actcaggaac	aagatgggca	agtggtgctg	ccactgcttc	540
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<210> 369

<211> 1853

<212> DNA

<213> Homo sapien

<400> 369

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<211> 2194

<212> DNA

<213> Homo sapien

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<212> DNA
<213> Homo sapien

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<212> DNA

<213> Homo sapien

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<211> 2000

<212> DNA

<213> Homo sapien

<400> 374

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<211> 2040

<212> DNA

<213> Homo sapien

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aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc 1320
aatggtgata atggattaat tcctcaaagg aagagcagaa cacctgaaaa tcagcaattt 1380
cctgaacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa 1440
aaacagatgc caaaatactc ttctgaaaac agcaaccag aacaagactt aaagctgaca 1500
tcagaggaag agtcacaaag gcttgagggc agtgaaaal ggcagccaga gaaaagatct 1560
caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa 1620
gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc 1680
actgctggca atggtgatga tggattaatt cctccaagga agagcagaac acctgaaagc 1740
cagcaatttc ctgacactga gaatgaagag tatcacagt acgaacaaaa tgatactcag 1800
aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1860
gaaaagcaga tagaagtggg tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa 1920
gaaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980
gagctagaca caatgaaaca tcagagtcag ctaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

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<210> 376

<211> 329

<212> PRT

<213> Homo sapien

<400> 376

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Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe
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Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
             20             25             30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
             35             40             45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
             50             55             60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65             70             75             80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
             85             90             95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
             100            105            110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
             115            120            125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
130            135            140

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Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
 145 150 155 160
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
 165 170 175
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
 180 185 190
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
 195 200 205
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
 210 215 220
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
 225 230 235 240
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
 245 250 255
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
 260 265 270
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
 275 280 285
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
 290 295 300
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
 305 310 315 320
 Ser Met Leu Phe Leu Val Ile Ile Met
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<210> 377

<211> 148

<212> PRT

<213> Homo sapien

<220>

<221> VARIANT

<222> (1)...(148)

<223> Xaa = Any Amino Acid

<400> 377

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 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
 20 25 30
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
 35 40 45
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
 50 55 60
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
 65 70 75 80
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
 85 90 95
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
 100 105 110
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp

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<210> 378
<211> 1719
<212> PRT
<213> Homo sapien
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	<400> 378														
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Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe
			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
		35					40					45			
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
65					70					75					80
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
				85					90					95	
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
			100					105					110		
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
		115					120				125				
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
	130				135						140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195					200						205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
	210					215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275				280						285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
	290					295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile

305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355					360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys
	370					375					380				
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser
385					390					395					400
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys
				405					410					415	
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly
			420					425					430		
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys
		435					440					445			
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly
	450					455					460				
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys
465					470					475					480
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys
				485					490					495	
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp
			500					505					510		
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu
		515					520					525			
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp
	530					535					540				
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln
545					550					555					560
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val
				565					570					575	
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn
			580					585					590		
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu
		595					600					605			
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp
	610					615					620				
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys
625					630					635					640
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys
				645					650					655	
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys

Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser
				725					730					735	
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln
			740					745					750		
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys
		755					760					765			
Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser
	770					775					780				
Gln	Pro	Glu	Lys	Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp
785					790					795					800
Arg	Glu	Val	Glu	Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly
			805						810					815	
Leu	Leu	Glu	Asn	Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn
			820					825					830		
Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe
		835					840					845			
Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser
	850					855					860				
Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn
865					870					875					880
Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu
			885						890					895	
Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile
			900					905					910		
Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn
		915					920					925			
Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro
	930					935						940			
Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu
945					950					955					960
Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe
			965						970					975	
Cys	Glu	Glu	Gln	Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His
			980					985					990		
Glu	Glu	Lys	Gln	Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser	Glu	Leu	Ser
		995					1000					1005			
Leu	Ser	Cys	Lys	Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn	Ser	Thr	Leu
	1010					1015					1020				
Arg	Glu	Glu	Ile	Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr	Met	Lys	His
1025					1030					1035					104
Gln	Ser	Gln	Leu	Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met
			1045						1050					1055	
Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met
			1060					1065					1070		
Gly	Lys	Trp	Cys</												

Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His				
			1140					1145					1150						
Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp				
			1155					1160					1165						
Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg				
			1170					1175					1180						
Gly	Glu	Asp	Leu	Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val				
1185						1190				1195						120			
Pro	Arg	Lys	Asp	Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys				
				1205					1210						1215				
Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly				
			1220					1225						1230					
Asn	Ser	Glu	Val	Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn				
			1235					1240					1245						
Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys				
			1250					1255				1260							
Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro				
1265						1270				1275						128			
Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr				
				1285					1290						1295				
Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp				
			1300					1305						1310					
Ile	Glu	Ser	Lys	Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val				
			1315					1320					1325						
His	Glu	Gln	Lys	Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala				
			1330					1335				1340							
Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala				
1345						1350				1355						136			
Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn				
				1365					1370						1375				
Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr				
			1380					1385						1390					
Ala	Val	Ser	Ser	His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr				
			1395					1400					1405						
Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu				
			1410					1415				1420							

Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu
 1540 1545 1550
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser
 1555 1560 1565
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe
 1570 1575 1580
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe
 1585 1590 1595 1600
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly
 1605 1610 1615
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro
 1620 1625 1630
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln
 1635 1640 1645
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile
 1650 1655 1660
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser
 1665 1670 1675 1680
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
 1685 1690 1695
 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr
 1700 1705 1710
 Met Lys His Gln Ser Gln Leu
 1715

<210> 379

<211> 656

<212> PRT

<213> Homo sapien

<400> 379

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1 5 10 15
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20 25 30
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35 40 45
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50 55 60
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65 70 75 80
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85 90 95
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
 100 105 110
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
 115 120 125
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
 130 135 140
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
 145 150 155 160

Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
		195					200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
	210					215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
	290					295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355					360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
		370				375					380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420					425					430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435					440					445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
		450				455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505					510		
Asn															

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<210> 380
<211> 671
<212> PRT
<213> Homo sapien
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	<400> 380															
Met 1	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys	
				5					10					15		
Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe	
			20					25					30			
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp	
		35				40					45					
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	
	50					55					60					
Cys 65	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val	
					70					75				80		
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn	
				85					90					95		
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	
			100					105					110			
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe	
			115				120					125				
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His	
	130					135					140					
Arg 145	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met	
					150					155				160		
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala	
				165					170					175		
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu	
			180					185					190			
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr	
		195					200					205				
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met	
	210					215					220					
Leu 225	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn	
					230					235				240		
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys	
				245					250					255		
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly	

			260						265						270					
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val					
		275					280					285								
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr					
	290					295					300									
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile					
305					310						315				320					
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu					
				325					330					335						
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val					
			340					345					350							
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile					
		355					360					365								
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu					
	370				375						380									
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys					
385				390						395					400					
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu					
				405					410					415						
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn					
			420					425					430							
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro					
		435					440					445								
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu					
	450					455					460									
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu					
465				470						475					480					
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp					
				485					490					495						
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu					
			500					505					510							
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp					
		515					520					525								
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys					
	530					535					540									
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala					
545				550						555					560					
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg					
				565					570					575						
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His					
			580					585					590							
Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe	Cys	Glu	Glu	Gln	Asn					
		595					600					605								

<210> 381
 <211> 251
 <212> DNA
 <213> Homo sapien

<400> 381
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt cctcaccaa 60
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg 120
 ccaatatccc aggagaagca ttggggaggt gggggcagggt gaaggacca ggactcacac 180
 atcctggggc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240
 caagcagtca g 251

<210> 382
 <211> 3279
 <212> DNA
 <213> Homo sapiens

<400> 382
 cttcctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
 cactgggagg ggacatcctg cagaaggtag gagtgcgaa acacccgctg caggggaggg 180
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ccgggagggag 240
 gggcctggag ggcgtgagga ggagcaggg ggctgcatgg ctggagttag ggatcagggg 300
 cagggcgcga gatggcctca cacagggaag agagggcccc tctgcaggg cctcacctgg 360
 gccacaggag gacactgctt ttccctctag gagtgcaggag ctgtggatgg tgctggacag 420
 aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540
 gtggctccag gccttgcccc tgcctggggc ctccccagc ctccctcaca gtctcctggc 600
 cctcagtctc tccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660
 gaactgacca taccagccc tgcccacggc cctccatggc tccccaatgc cctggagagg 720
 ggacatctag tcagagagta gtcctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
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 gagccttggt cctctgttg gactccctgc ccatattctt gtgggagtgg gttctggaga 960
 cattctgtc tgttctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020
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 tgtttgtggg gtgcagagat gggaggggtg gggccacccc tggaagagtg gacagtga 1620
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 acacacagca aggttgacgc tgtaaacata gccacgctg tcctgggggc actgggaagc 1740
 ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgtgttg aaggagggag 1800
 tagggggaga aactgaaagc tgattaatta caggaggttt gttcaggtcc cccaaaccac 1860
 cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggg 1920


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ttattatggt ttgttacatt gataggatag atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgagtt acgaagactg gcaacttggc 2040
tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgata cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
caaggatgta tgataatatg tacaaagtaa ttccaactga ggaagctcac ctgaccccta 2280
gtgtccaggg tttttactgg gggctctgtg gacgagtatg gactacttga ataattgacc 2340
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cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

```

<210> 383

<211> 155

<212> PRT

<213> Homo sapiens

<400> 383

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Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5                      10                      15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                      25                      30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                      40                      45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                      55                      60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                      70                      75                      80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                      90                      95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                     105                     110

```

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
 115 120 125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
 130 135 140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
 145 150

<210> 384

<211> 557

<212> DNA

<213> Homo sapiens

<400> 384

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ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggt cctttttgca ttgccaagtg ccataacct gagcactact ctaccatggg 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tccccaaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaa aaaaaaa 557

```

<210> 385

<211> 337

<212> DNA

<213> Homo sapiens

<400> 385

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ttcccagggtg atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
tctcaaagcc atctgctgtc ttcgagtaag gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgetggtt ccctgtcgtg gtctggatct 300
ctttggccac caattcccc tttccacat cccggca 337

```

<210> 386

<211> 300

<212> DNA

<213> Homo sapiens

<400> 386

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gggcccgccta ccggcccagg cccgcctcg cgagtctctc tccccgggtg cctgcccgc 60
gccgcctcgg ccagaggggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcggc 180
gcggactttg cccggtgtgt gggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgtgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

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<210> 387
 <211> 537
 <212> DNA
 <213> Homo sapiens

<400> 387
 gggccgagtc gggcaccaag ggactctttg caggcttctt tcctcggatc atcaaggctg 60
 cccctctctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
 tgaaccagga ccggcttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
 ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
 gagggggctt gtttcccttc cctcccggcg acaagctcca gggagaggct gtccctctgg 300
 gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360
 cttaccacc ccccaagttc aagaacaaat ctccagctg ccccttcgt gtttccctgt 420
 gtttgctgta gctgggcatg tctccaggaa ccagaagcc ctccagctgg tgtagtctcc 480
 ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaaa aaaaaaa 537

<210> 388
 <211> 520
 <212> DNA
 <213> Homo sapiens

<400> 388
 aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
 tgagggttaaa ccagtttgca ttcccctaatt gtggaaaaag taagaggact actcagcact 120
 gtttgaagat tgccctctct acagcttctg agaatttgtt tatttcactt gccagtgaa 180
 ggacccccct cccaacatgc cccagccccc cctaagcat ggtcccttgt caccaggcaa 240
 ccaggaaaact gctacttgtg gacctacca gagaccagga gggtttggtt agctcacagg 300
 acttccccca cccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
 tcatactcaa ttgatggta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
 atctttctct ttctcattac cagtaaaggc tcttgggtatc tttctgttgg aatgatttct 480
 atgaacttgt cttattttta tgggtgggtt ttttctggt 520

<210> 389
 <211> 365
 <212> DNA
 <213> Homo sapiens

<400> 389
 cgttgccccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
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 aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
 aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtcctcac agctgagact 240
 cccaggaaac cttcagacta ctttctctg cttcagcaa gggcggttc ccacattctc 300
 tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
 gggag 365

<210> 390
 <211> 221
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(221)
 <223> n = A,T,C or G

<400> 390
 tgcctctcca tccctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
 tacacggntt ctcctgggtg tggaacatct ctgcttgagg ttccaggaag gcctctggct 120
 gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
 tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

<210> 391
 <211> 325
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(325)
 <223> n = A,T,C or G

<400> 391
 tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
 ctctcgcgcc cagcctggag ctgctcctgg catctacca caatcagncg aggcgagcag 120
 tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
 naantngat ntccanagcc ctaccatcn tagttctgct ctcccacgg ntaccagccc 240
 cactgcccag gaatctaca gccagtacc tgtcccgacg tctctaccta ccagtacgat 300
 gagacctccg gctactacta tgacc 325

<210> 392
 <211> 277
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(277)
 <223> n = A,T,C or G

<400> 392
 atattgttta actccttcct ttatatcttt taacattttc atgngaaaag gttcacatct 60
 agtctcactt ngcnagnn ctcctacttg agtctcttcc ccggcctggn ccagtngnaa 120
 antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
 tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
 ctgaggatag agcgccgcgt cctgtgttgc tggggaa 277

<210> 393
 <211> 566
 <212> DNA
 <213> Homo sapiens

<400> 393

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actagtcacag tgtggtggaa ttgcgggccc cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga tttaaattcag cctaaacggt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatataa ggactgggta cttgggtaag 240
gaggggtcta ggagatctgt ccccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtgggttt caaaagtaga aatgtcctgt attccgatga tcacccctga aacattttat 360
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ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttggtg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaaa aaaaaa 566

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<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(384)

<223> n = A,T,C or G

<400> 394

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gaacatacat gtcccgccac ctgagctgca gctcgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggctggact gctggagcgt gtgaaggagc racaggccna 120
gcaggaggac cgggctttta ggagttttta gctygagtgc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atcgggttgg agcatgacgt 240
gaacatccag ttctctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384

```

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

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ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60
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tatcagaggt ttcacattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
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ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagtctctt ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggg 360
gcagcctggg gagaccatcc aatcccaat aaaatgcac 399

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<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(403)
 <223> n = A,T,C or G

<400> 396
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 agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
 actaaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
 taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
 gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
 atcaaagcag gtgctatcac tcaatgttag gcctgctct ttt 403

<210> 397
 <211> 100
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(100)
 <223> n = A,T,C or G

<400> 397
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 tccatccccg ctctgggttg gtnacagaat gactgacaaa 100

<210> 398
 <211> 278
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(278)
 <223> n = A,T,C or G

<400> 398
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 ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
 tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
 ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
 ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399
 <211> 298
 <212> DNA
 <213> Homo sapiens

<220>

<221> misc_feature
 <222> (1)...(298)
 <223> n = A,T,C or G

<400> 399
 acggaggtgg aggaagcgnc cctgggatcg anaggatggg tectgncatt gaccncctcn 60
 ggggtgccng catggagcgc atggggcgcg gcctgggcca cggcatggat cgcgtgggct 120
 ccgagatcga gcgcattyggc ctggtcattgg accgcattgg ctcctgggag cgcattgggt 180
 ccggcattga gcgcattyggc ccgctgggccc tcgaccacat ggcctccanc attgancgca 240
 tgggcccagac catggagcgc attgggtctcg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400
 <211> 548
 <212> DNA
 <213> Homo sapiens

<400> 400
 acatcaacta cttcctcatt ttaaggtatg gcagttccct tcateccctt ttcctgcctt 60
 gtacatgtac atgtatgaaa ttcccttctc ttaccgaact ctctccacac atcacaaggt 120
 caaagaacca caccgttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
 tgagtctctt ttttccacgt ttaagggggc atggcaggac ttagagttgc gaggtaagac 240
 tgcagagggc tagagaatta ttctctacag gctctgaggc caccatgtc acttatcccg 300
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
 gttggcccca taattctggg cttttgttgt ttgttttaac tacttgggca tcccaggaag 420
 ctttccagtg atctcctacc atggggcccc ctcttgggat caagcccttc ccaggccctg 480
 tccccagccc ctcttgcccc agcccaccgg cttgccttgg tgctcagccc tcccattggg 540
 agcaggtr 548

<210> 401
 <211> 355
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(355)
 <223> n = A,T,C or G

<400> 401
 actgtttcca tggtatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
 tgatgtctcc aagtagtcca ctttcattta actctttgaa actgtatcat ctttgccaag 120
 taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
 tataaatgaa tgtgctgaag caaagtgcc atgggtggcg cgaagaagan aaagatgtgt 240
 tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggg 300
 cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

<210> 402
 <211> 407
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(407)
 <223> n = A,T,C or G

<400> 402
 atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
 tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
 aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
 gaataaagat aaaaaagaga aggacattac aaaggtgggc ctgacctttg ataaatctca 240
 ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa ttgctgagg 300
 ttgtggagct tctccctgc agagagtcctc tgatctccca aaatttggtt gagatgtaag 360
 gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407

<210> 403
 <211> 303
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 403
 cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaattc aggcacccaa 60
 tcttaagcaa gagccatggc atgggtgaaaa tgcaaaaggga gagtctggcc aatctacaaa 120
 tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
 gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
 tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300
 gga 303

<210> 404
 <211> 225
 <212> DNA
 <213> Homo sapiens

<400> 404
 aagtgtaaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
 attgttaatg cactcattta cttttacatg gtgaaagtct tctcttgatc ctacaaacag 120
 acattttcca ctctgttttc catagttggt aagtgtatca gatgtgttgg gcatgtgaat 180
 ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcac 225

<210> 405
 <211> 334
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaa at ctgaggggtt tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctagge 180
ttcccagtg cttccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgctctca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

```
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggtc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aattnnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaa atgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

<400> 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
cttctctcaa ggngaggcaa a 261

```

```

<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(241)
<223> n = A,T,C or G

```

```

<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcaactgggtg cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241

```

```

<210> 413
<211> 231
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

```

```

<400> 413
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtag cttctctttg ttgtgaagga taarcaaact gaacaacaaa 120
aagtttactc tcttcatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

```

```

<210> 414
<211> 234
<212> DNA
<213> Homo sapiens

```

```

<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggg cttccttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaaagctga ttcactatgg ggggaggtgt attgaagtcc tcca 234

```

```

<210> 415

```

<211> 217
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(217)
 <223> n = A,T,C or G

<400> 415
 gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
 caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
 cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
 antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416
 <211> 213
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(213)
 <223> n = A,T,C or G

<400> 416
 atgcatatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
 ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
 cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
 atattggaac agatggagtc tctactacaa aag 213

<210> 417
 <211> 303
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 417
 nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
 gtgggaaagg ctttactctg agttcaaate ttcaagcca tcagagagtc cacactggag 120
 agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
 ttcatttagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggtc 240
 tcantcaaag ttogtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
 agt 303

<210> 418
 <211> 328

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
t t t t t g g c g g t g g t g g g c a g g g a c g g g a c a n g a g t c t c a c t c t g t t g c c c a g g c t g g a g 60
t g c a c a g g c a t g a t c t c g g c t c a c t a c a a c c c c t g c c t c c a t g t c c a a g c g a t t c t t g t 120
g c c t c a g c c t t c c c t g t a g c t a g a a t t a c a g g c a c a t g c c a c c a c a c c a g c t a g t t t t t 180
g t a t t t t t a g t a g a g a c a g g g t t t c a c c a t g t t g g c c a g g c t g g t c t c a a a c t c c t n a c c 240
t c a g n g g t c a g g c t g g t c t c a a a c t c c t g a c c t c a a g t g a t c t g c c c a c c t c a g c c t c c c 300
a a a g t g c t a n g a t t a c a g g c c g t g a g c c 328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
c c t c c t c a a g a c g g c c t g t g t c c g c c t c c c g g c a a c c a a g a a g c c t g c a g t g c c a t a t g 60
a c c c c t g a g c c a t g g a c t g g a g c c t g a a a g g c a g c g t a c a c c c t g c t c c t g a t c t t g c t g 120
c t t g t t t c c t c t c t g t g g c t c c a t t c a t a g c a c a g t t g t t g c a c t g a g g c t t g t g c a g g c 180
c g a g c a a g g c c a a g c t g g c t c a a a g a g c a a c c a g t c a a c t c t g c c a c g g t g t g c c a g g c a 240
c c g g t t c t c c a g c c a c c a a c t c a c t c g c t c c c g c a a a t g g c a c a t c a g t t c t t c t a c c c 300
t a a a g g t a g g a c c a a a g g g c a t c t g c t t t t c t g a a g t c c t c t g c t c t a t c a g c c a t c a c g 360
t g g c a g c c c a c t c n g g c t g t g t c g a c g c g g 389

<210> 420
<211> 408
<212> DNA
<213> Homo sapiens

<400> 420
g t t c c t c c t a a c t c c t g c c a g a a c a g c t c t c c t c a a c a t g a g a g c t g c a c c c c t c c t c c 60
t g g c c a g g g c a g c a a g c c t t a g c c t t g g c t t c t t g t t t c t g c t t t t t t c t g g c t a g a c c 120
g a a g t g t a c t a g c c a a g g a g t t g a a g t t t g t g a c t t t g g t g t t c g g c a t g g a g a c c g a a 180
g t c c c a t t g a c a c t t t c c c a c t g a c c c c a t a a g g a a t c c t c a t g g c c a c a a g g a t t t g 240
g c c a a c t c a c c a g c t g g g c a t g g a g c a g c a t t a t g a a c t t g g a g a g t a t a t a a g a a a g a 300
g a t a t a g a a a a t t c t t g a a t g a g t c c t a t a a c a t g a a c a g g t t t a t a t t c g a a g c a c a g 360
a c g t t g a c c g g a c t t t g a t g a a g t g c t a t g a c a a a c c t g g c a a g c c c g 408

<210> 421
<211> 352

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(352)
<223> n = A,T,C or G

<400> 421
gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352

<210> 422
<211> 337
<212> DNA
<213> Homo sapiens

<400> 422
atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtgggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337

<210> 423
<211> 310
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggccctggcct gggagccctg tgccctactan aagcncatta gattatccat 120
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta 310

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(370)
 <223> n = A,T,C or G

<400> 424
 gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
 ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
 cactgacaga acaggtcttt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
 ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
 ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
 cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
 tccgtcgacg 370

<210> 425
 <211> 216
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(216)
 <223> n = A,T,C or G

<400> 425
 aattgctatn nttttatttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaataga 60
 taacaacnca acatcaaggc aananaaca ggaatggntg actntgcata aatnggccga 120
 anattatcca ttatnttaag ggttgacttc aggttacagc acacagacaa acatgcccgag 180
 gaggntntca ggaccgctcg atgtntntg agggagg 216

<210> 426
 <211> 596
 <212> DNA
 <213> Homo sapiens

<400> 426
 cttccagtga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60
 tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggc tcgctggcca 120
 gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180
 gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
 gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtta 300
 ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
 aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
 ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
 atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggct tactgcctga 540
 gtcccgtcgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427
 <211> 107
 <212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

gaacttcna anaangactt tattcactat ttacatt 38

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttccact tcagttacac ctactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat 544

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G


```

<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccctgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttggt atctttgcn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactcran aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagtct tgtgtgtgga gtcttgggtt ttccaacaga 240
catcartcca gcattctgag attagggnga ttggggatca ttcrggagtt ggaatgttca 300
acaaaagtga tgttggttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggctttttac tctgctgttt ct 392

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgna gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

```

<210> 433
<211> 281

```

<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

<400> 433
ttcaactagc anagaanact gcttcagggg gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagngagg ntctctgtnt gccactggg 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

<210> 434
<211> 484
<212> DNA
<213> Homo sapiens

<400> 434
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc ccctcctctg 60
aatttaattc ttccaacttg caatttgcaa ggattacaca ttccactgtg atgtatattg 120
tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaaccat ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccr 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttta 484

<210> 435
<211> 424
<212> DNA
<213> Homo sapiens

<400> 435
gcgccgctca gaggaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcaggtgtc ggggtgaccc 240
cttgagaga ggaaaaaggc cacaagaggg gctgccaccg cactaacgg agatggccct 300
ggtagagacc ttggggggtc tggaaacctt ggactcccca tgccttaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

<210> 436
<211> 667
<212> DNA
<213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(667)
 <223> n = A,T,C or G

<400> 436
 accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
 tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggggtgc 120
 agcctcttct ggaattcctc tgatttcaaa gtctcactct caagtctctg aaaacgaggg 180
 cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
 atgggctgcc agagtaggat aggattccag atgctgacac ctctggggg aaacaggggt 300
 gccaggtttg tcatagcact catcaaagtc cggctcaacgt ctgtgcttcg aatataaacc 360
 tgttcatggt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
 agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
 gattccttta tggggtcagt gggaaagggt tcaatgggac ttcgggtctcc atgccgaaac 540
 accaaagtca caaacttcaa ctcttggtggt agtacacttc ggtctagcca gaaaaaaagc 600
 agaaacaaga agccaagggt aaggcttgct gcctgccag gaggaggggt gcagctctca 660
 tgttgag 667

<210> 437
 <211> 693
 <212> DNA
 <213> Homo sapiens

<400> 437
 ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
 acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
 taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
 ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
 aggtactcct ctattttcac cctcttgct tctactctct ggcagtcaga cctgtgggag 300
 gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
 catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
 atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
 acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
 tcctatttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatctgttt 600
 taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
 ctgcatcatg tgctctcttg gctgaaaatg acc 693

<210> 438
 <211> 360
 <212> DNA
 <213> Homo sapiens

<400> 438
 ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
 ttatgcaatg catcatgcta tttcatacct aatgaggagg ttccaggaga ttcaaccagg 120
 atgtttctac acctgtgggt tatgacaaaag acaactgcc aagaatcttc aagaaggagg 180
 actgcaagta tatctggtgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
 gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
 gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439
 <211> 431
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(431)
 <223> n = A,T,C or G

<400> 439
 gttcctnnta actcctgcca gaaacagctc tcttcaacat gagagctgca cccctcctcc 60
 tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
 gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180
 gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
 gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
 gatatagaaa attcttgaat gagtccctata aacatgaaca ggtttatatt cgaagcacag 360
 acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
 aatttagtag t 431

<210> 440
 <211> 523
 <212> DNA
 <213> Homo sapiens

<400> 440
 agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
 ggatcttttg tatitaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaacc cacaatctag ggtgggaaca 180
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240
 cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
 actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
 taaaaattaa aacctctttg tgtcccttgg tcttggaaca tttatgttcc ttttaaagaa 420
 acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480
 tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441
 <211> 430
 <212> DNA
 <213> Homo sapiens

<400> 441
 gttcctccta actcctgcca gaaacagctc tcttcaacat gagagctgca cccctcctcc 60
 tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
 gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180
 gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
 gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
 gatatagaaa attcttgaat gagtccctata aacatgaaca ggtttatatt cgaagcacag 360
 acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
 aatttagtag 430

<210> 442
 <211> 362
 <212> DNA
 <213> Homo sapiens

<400> 442
 ctaaggaatt agtagtggtc ccatacacttg tttggagtggt gctatttctaa aagatttttga 60
 tttcctggaa tgacaattat attttaactt tgggtggggga aagagttata ggaccacagt 120
 cttcactttct gatacttgta aattaatctt ttattgcact tgttttgacc attaaagctat 180
 atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
 aatgaattaa tgttttactt aattttatatt gaactgtcaa tgacaaataa aaatttctttt 300
 tgattattttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
 tc 362

<210> 443
 <211> 624
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(624)
 <223> n = A,T,C or G

<400> 443
 tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
 ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
 aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcagggtacc ctgccttttg 180
 tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
 cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
 tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaataaac 360
 taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtag 420
 atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaag 480
 agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
 ngatgcttgt gctgggtcca aatcttgggc tactatgacc ttggccaaat tatttaaact 600
 ttgtccctat ctgctaaaca gatc 624

<210> 444
 <211> 425
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(425)
 <223> n = A,T,C or G

<400> 444
 gcacatcatt nntcttgcac tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
 gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaaatg aacaagtaag 120
 ttcattgcta tagcataaca caaaatttgc ataagtgggt gtcagcaaat ccttgaatgc 180

```

tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttggttt tgcctcctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggctgacg cggccgcgaa tttagtagta 420
gtaga                                         425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtggc agattattgg atgtagtctt ctttaactag catataaatc 180
tgggtgtgtt cagataaatg aacagcaaaa tgtgggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaagtact aggtctctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaaa tgcagcggc cgcgaattta gtag          414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaccttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttggtgtg 540
aatctacacc aatgaaaaca tgtactacag ctatatgtga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g                                     631

```

```

<210> 447
<211> 585
<212> DNA

```

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat ctccagaaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcattgtt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcgggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg tcattctgan nnccgaactg acctgcccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

```
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggctggggc cgtccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcgggt cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
```

```

cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccncaactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggagggttc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

```

```

<210> 450
<211> 493
<212> DNA
<213> Homo sapiens

```

```

<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaaa aacataaaaa gaaatatacct atagtggaaa taagagagtc 120
aatgagggtc gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcggcc 480
gcgaatttag tag 493

```

```

<210> 451
<211> 501
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

```

```

<400> 451
gggcccgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaagggcat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgcag gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatacnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncacagc actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggccnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

```

<210> 452
<211> 51
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(51)

```


<223> n = A,T,C or G

<400> 452

agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453

<211> 317

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(317)

<223> n = A,T,C or G

<400> 453

tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaaccat 120
ttcaccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccacaaac tttatTTTTT tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
taccatgtc tttatta 317

<210> 454

<211> 231

<212> DNA

<213> Homo sapiens

<400> 454

ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cagctcttg aaggagtctt gaattctctt ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttctttt tcagtgttcc aaagctcttc acaatttcat gaacaacagc t 231

<210> 455

<211> 231

<212> DNA

<213> Homo sapiens

<400> 455

taccaagag ggcataataa tcagtctcac agtagggttc accatctctc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcttttg gcacgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggtctc tttctctct a 231

<210> 456

<211> 231

<212> DNA

<213> Homo sapiens

<400> 456

```

ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcggtt attattcttg gagaaaccct gtctgtttac tgtaaccctt 120
tgcactcaaa ttccctttatc aggaataact acatagccac tatttacaaa gccattggaa 180
cctttttatt tgggtgcagct gctagtcagt ccttgactga cattgccaag t 231

```

<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

```

cgaggtagcc aggggtctga aaatctctnn ttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgctt catttctctt gaggtgtcgc tggcttttgt g 231

```

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

```

aggtctggtt cccccactt ccactccctt ctactctctt taggactggg ctgggcccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccacctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggcccag accccaggag aagaagattc t 231

```

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

```

ggtaccgagg ctgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gccaccagt cctaacggga caggacagag agacagagca 120
gcctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

```

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

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<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

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gtgggggttca gtgaggagtg ggaaattggg tcagcagaac caagccgttg ggtgaataag 180
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<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

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gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
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<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

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<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
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<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

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<400> 465

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<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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cctgtgcaat caaatattgt ggagaattcc ctactgtggag aagtcacaaa gactatagga 180
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<210> 467

<211> 311

<212> DNA

<213> Homo sapiens

<400> 467

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<210> 468

<211> 3112

<212> DNA

<213> Homo sapiens

<400> 468

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<210> 469

<211> 2229

<212> DNA

<213> Homo sapiens

<400> 469

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aagtatatta tataagatac tatgaggttc cctgcctttg cttcacatcc caggcttaca 300
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<210> 470

<211> 2426

<212> DNA

<213> Homo sapiens

<400> 470

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2426

<210> 471

<211> 812

<212> DNA

<213> Homo sapiens

<400> 471

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812

<210> 472
 <211> 515
 <212> DNA
 <213> Homo sapiens

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<400> 472
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 <211> 5829
 <212> DNA
 <213> Homo sapiens

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<210> 474

<211> 1594

<212> DNA

<213> Homo sapiens

<400> 474

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<212> DNA

<213> Homo sapiens

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<211> 3434
<212> DNA
<213> Homo sapiens

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<211> 141

<212> PRT

<213> Homo sapiens

<400> 477

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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
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Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
35 40 45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
50 55 60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
65 70 75 80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
85 90 95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
100 105 110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val

115 120 125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
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<210> 478
<211> 144
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Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
85 90 95

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
100 105 110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
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His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
130 135 140

<210> 479
<211> 223
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
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Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
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Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
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Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
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Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
210 215 220

<210> 480

<211> 145

<212> PRT

<213> Homo sapiens

<400> 480

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5 10 15

Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
20 25 30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg

35 40 45
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
 50 55 60
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
 65 70 75 80
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
 85 90 95
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
 100 105 110
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
 115 120 125
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
 130 135 140

<210> 481

<211> 168

<212> PRT

<213> Homo sapiens

<400> 481

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Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
 20 25 30

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
 35 40 45

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
 50 55 60

Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro
 65 70 75 80

Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
 85 90 95

Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala
 100 105 110

1
2
3
4
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<213> Homo sapiens

<400> 483

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Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15

Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30

Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45

Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60

Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80

Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95

Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110

Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125

Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

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<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

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Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1              5              10              15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

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<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

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<210> 486
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 <212> DNA
 <213> Artificial Sequence

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<400> 486
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<210> 487
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 487
 cccgaattct tagctgccc tccgaacgcc ttcata 36

<210> 488
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 488
 gggaagcttc ttccccggct gcaccagctg tgc 33

<210> 489
 <211> 19
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 489
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
 1 5 10 15
 Ser Val Ala

<210> 490
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Made in a lab

<400> 490

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Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
 1              5              10              15
Leu Ser His Ser
              20

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<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

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Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
 1              5              10              15
Thr Gly Phe Thr
              20

```

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

```

Ala Leu Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr
 1              5              10              15
Leu Ala Ser Leu
              20

```

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

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Tyr Thr Leu Ala Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro
 1              5              10              15
Lys Tyr Arg Gly
              20

```

<210> 494
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 494
 Leu Pro Lys Tyr Arg Gly Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser
 1 5 10 15
 Leu Met Ile Ser
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<210> 495
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 495
 Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
 1 5 10 15
 Phe Pro Asn Gly
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<210> 496
 <211> 21
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 496
 Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
 1 5 10 15
 Pro Pro Pro Pro Ala
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<210> 497
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 497
 Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
 1 5 10 15
 Ser Val Arg Val
 20

<210> 498
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 498
 Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
 1 5 10 15
 Val Pro Gly Arg
 20

<210> 499
 <211> 20
 <212> PRT
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<220>
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<400> 499
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
 1 5 10 15
 Ser Ala Phe Leu
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<210> 500
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 500
 Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
 1 5 10 15
 Gly Ser Ile Val
 20

<210> 501
 <211> 20

<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 501
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
1 5 10 15
Val Ser Ala Ala
20

<210> 502
<211> 414
<212> DNA
<213> Homo Sapien

<400> 502
caccatggag acaggcctgc gctggctttt cctggctcgt gtgctcaaag gtgtccaatg 60
tcagtcggtg gaggagtccg ggggtcgccct ggtcacgcct gggacacctt tgacantcac 120
ctgtagagtt tttggaatng acctcagtag caatgcaatg agctgggtcc gccaggctcc 180
aggggaagggg ctggaatgga tcggagccat tgataattgt ccacantacg cgacctgggc 240
gaaaggccga tttnatnattt ccaaaacctn gaccacgggtg gatttgaaaa tgaccagtcc 300
gacaaccgag gacacggcca cctatttttg tggcagaatg aatactggta atagtggttg 360
gaagaatatt tggggcccag gcaccctggt caccgtntcc tcagggcaac ctaa 414

<210> 503
<211> 379
<212> DNA
<213> Homo Sapien

<400> 503
atnccgatggt gcttgggtcaa aggtgtccag tgtcagtcgg tggaggagtc cgggggtcgc 60
ctgggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt 120
agctatggag tgagctgggt ccgccaggct ccagggaagg ggctggnata catcggtatca 180
ttagtagtag tggtagattt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa 240
cctngaccac ggtggatttg aaaatcacca gtttgacaac cgaggacaug gccacctatt 300
tntgtgccag agggggggtt aattataaag acatttgggg cccaggcacc ctgggtcaccg 360
tntccttagg gcaacctaa 379

<210> 504
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 504
Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu

1 5 10 15
Asn Ser Ala

<210> 505
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 505
Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
1 5 10 15
Asn Thr Ala Asn
20

<210> 506
<211> 407
<212> DNA
<213> Homo Sapien

<400> 506
atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaagggtgt ccagtgtcag 60
tcgctggagg agtccggggg tcgcctgggc acgcctggga cacccttgac actcacctgc 120
accgtctctg gattctccct cagtagcaat gcaatgatct gggtcgcgca ggctccaggg 180
aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg 240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg 360
ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa 407

<210> 507
<211> 422
<212> DNA
<213> Homo Sapien

<400> 507
atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaagggtgt ccagtgtcag 60
tcggtggagg agtccggggg tcgcctgggc acgcctggga cacccttgac actcacctgt 120
acagtctctg gattctccct cagcaactac gacctgaact gggtcgcgca ggctccaggg 180
aaggggctgg aatggatcgg gatcattaat tatgttggta ggacggacta cgcgaactgg 240
gcaaaaggcc ggttcaccat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300
ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360
ggcccggtgct tgcgcctctg gggcccaggc accctgggtca ccgtctcctt agggcaacct 420
aa 422

<210> 508
<211> 411
<212> DNA
<213> Homo Sapien

<400> 508
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 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccagga 180
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 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360
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<210> 509
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 509
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 1 5 10 15

<210> 510
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 510
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
 1 5 10 15

<210> 511
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
 1 5 10 15

<210> 512
 <211> 15
 <212> PRT
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CGTCTCCTTG

<220>

<223> Made in a lab

<400> 512

Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu
1				5					10					15

<210> 513

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 513

Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Asx	Val	Tyr	Thr	Asn	Leu
1				5					10					15

<210> 514

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 514

Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser
1				5					10					15

<210> 515

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 515

Met	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg
1				5					10					15

<210> 516

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

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<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

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<223> Made in a lab

<400> 519

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<211> 25

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

<400> 520
 Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
 1 5 10 15
 Glu Ala Arg Arg His Tyr Asp Glu Gly
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<210> 521
 <211> 21
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 521
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 1 5 10 15
 Pro Pro Pro Pro Ala
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<210> 522
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
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<400> 522
 Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
 1 5 10 15
 Phe Thr Gln Val
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<210> 523
 <211> 254
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Made in a lab

<400> 523
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
 1 5 10 15
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
 20 25 30
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
 35 40 45
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
 50 55 60

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Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
 65 70 75 80
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
 85 90 95
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
 100 105 110
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
 115 120 125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
 130 135 140
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
 145 150 155 160
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
 165 170 175
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
 180 185 190
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
 195 200 205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
 210 215 220
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
 225 230 235 240
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
 245 250

<210> 524
 <211> 765
 <212> DNA
 <213> Homo sapien

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 <213> Homo sapien

<400> 525

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Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
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Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
      50           55           60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
      65           70           75           80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
      85           90           95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
      100          105          110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
      115          120          125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
      130          135          140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
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Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
      165          170          175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
      180          185          190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
      195          200          205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
      210          215          220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
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Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
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<211> 963

<212> DNA

<213> Homo sapiens

<400> 526

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<213> Homo sapiens
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Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val
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Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
      50              55              60

Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
      65              70              75              80

Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
      85              90              95

Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
      100             105             110

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
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Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
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Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
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Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
      165             170             175

Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
      180             185             190

Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val

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 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
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 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
 225 230 235 240
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
 245 250 255
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
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 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
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<213> Homo Sapien

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<212> DNA

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<210> 530

<211> 1852

<212> DNA

<213> Homo sapiens

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<211> 879

<212> DNA

<213> Homo sapiens

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<211> 293

<212> PRT

<213> Homo sapiens

<400> 532

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Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
      35                      40                      45

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
      50                      55                      60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
      65                      70                      75                      80

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
      85                      90                      95

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
      100                     105                     110

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
      115                     120                     125

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
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Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
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Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
      165                     170                     175

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
      180                     185                     190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
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Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
      210                     215                     220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
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Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
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 115 120 125
 Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
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 Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
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 Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
 210 215 220
 Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
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<211> 6082

<212> DNA

<213> Homo sapiens

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Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val
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cctataatgg ggatctttca ctcaccctaa agtgaggaca aaatacttga aagcatgagc 3900
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aaaaaaaaa 4809

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<210> 570

<211> 951

<212> DNA

<213> Homo sapiens

<400> 570

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<210> 571

<211> 819

<212> DNA

<213> Homo sapiens

<400> 571

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ttattgcttt tgttgcaaat gccgtggctt catctgagga attctagaat tcagagggtg 180
tagccctcca ctctgctgtc ttgctatctg ctctcattgc atccgtttta cctgcattct 240

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acttgctcta ttgtctttta atttctgcct gttctttatg gctttcaact tcataaataa 420
catgttttct caaatctctt tgtgaattcc agagagggcc aggcacggtg gctcacatct 480
gtaatccag cactttgggg aggctgagac gggaggatca cttgaggtca ggagtttgag 540
accagcctgg ccaacatggt gaaatcccgt ttcactaaaa atacaaaaat taccaggca 600
tggtggcggg cgcctgtaat ccaggtact cgggaggctg agggaggaga atcgcttgaa 660
cctgggagga tgaggaggga gaatcgctt aaccggggag gcagaggttg cagtgaaccg 720
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<210> 572
 <211> 203
 <212> DNA
 <213> Homo sapiens

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<400> 572
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atcaggtctc atgagaactc atg 203

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<210> 573
 <211> 132
 <212> PRT
 <213> Homo sapiens

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<400> 573
Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
      5              10              15

Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
      20              25              30

Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35              40              45

Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50              55              60

Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65              70              75              80

Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85              90              95

Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100             105             110

Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115             120             125

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Leu Leu Asn Tyr
130

<210> 574
<211> 63
<212> PRT
<213> Homo sapiens

<400> 574
Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
5 10 15

His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
20 25 30

Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
35 40 45

Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
50 55 60

<210> 575
<211> 77
<212> PRT
<213> Homo sapiens

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
5 10 15

Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
20 25 30

Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
35 40 45

Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
50 55 60

Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
65 70 75

<210> 576
<211> 69
<212> PRT
<213> Homo sapiens

<221> unsure

<223> Xaa = Any Amino Acid

<400> 576

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr

Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
20 25 30

Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
35 40 45

Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
50 55 60

Pro Gly Tyr Ser
65

<210> 577

<211> 58

<212> PRT

<213> Homo sapiens

<400> 577

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
5 10 15

Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
20 25 30

Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
35 40 45

Arg Leu Ala Pro Pro Ala Asp Thr Pro
50 55

<210> 578

<211> 52

<212> PRT

<213> Homo sapiens

<400> 578

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
5 10 15

His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr

30

Gln Pro His
50

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<210> 579
<211> 57
<212> PRT
<213> Homo sapiens
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<400> 579
Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
5 10 15

Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
20 25 30

Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
35 40 45

Ile Ala Lys Val Tyr Gln Pro His
50 55

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<210> 580
<211> 68
<212> PRT
<213> Homo sapiens
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<400> 580
Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
5 10 15

Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
20 25 30

Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
35 40 45

His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
50 55 60

Phe Ile His
65

<210> 581

<211> 78
 <212> PRT
 <213> Homo sapiens

<400> 581
 Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
 5 10 15
 Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
 20 25 30
 Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
 35 40 45
 Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
 50 55 60
 Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
 65 70 75

<210> 582
 <211> 52
 <212> PRT
 <213> Homo sapiens

<400> 582
 Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
 5 10 15
 Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
 20 25 30
 Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
 35 40 45
 Leu Gly Val
 50

<210> 583
 <211> 61
 <212> PRT
 <213> Homo sapiens

<400> 583
 Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
 5 10 15
 Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
 20 25 30

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$\langle 210 \rangle$	586
$\langle 211 \rangle$	61

<212> PRT

<213> Homo sapiens

<400> 586

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
 5 10 15

Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
 20 25 30

Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
 35 40 45

Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
 50 55 60

<210> 587

<211> 1408

<212> DNA

<213> Homo sapiens

<400> 587

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cggctggaat tgctctgggt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaacagaa 300
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aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggtcttgg 420
agaaactagt caaaaggaga catccacctg tgatatttgc cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatattgac tgttctcaaa ccaacttcaa 540
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caaattagaa gaaagtgcc aagaacacca cataccttgt ccggaacatt acaatggctt 780
ctgcatgcat ggggaagtgtg agcattctat caatatgcag gagccatctt gcagggtgtga 840
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cggtcctgta cgatttcagt atgtcttaac cgcagctgtg attggaacaa ttcagattgc 960
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tacagtatta tagacaaaag aataagacaa gagatctaca catgttgctt tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatattt gattatgtat ggatatattt 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320
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aaaaaaaaaa aaaaaaaaaa rwmgaccc 1408

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<210> 588

<211> 81

<212> PRT

<213> Homo sapiens

<400> 588

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
5 10 15

Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
20 25 30

Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
35 40 45

Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
50 55 60

Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
65 70 75 80

Ile

<210> 589

<211> 157

<212> PRT

<213> Homo sapiens

<400> 589

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
5 10 15

Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
20 25 30

Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu
35 40 45

Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
50 55 60

Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
65 70 75 80

Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
85 90 95

Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
100 105 110

Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
115 120 125

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Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
 130 135 140

Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
 145 150 155

<210> 590

<211> 347

<212> PRT

<213> Homo sapiens

<400> 590

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
 5 10 15

Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
 20 25 30

Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
 35 40 45

Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
 50 55 60

Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
 65 70 75 80

Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
 85 90 95

Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
 100 105 110

Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
 115 120 125

Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
 130 135 140

Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
 145 150 155 160

Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
 165 170 175

Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
 180 185 190

Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr Thr

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195					200					205						
Lys	Ser	Glu	Asp	Gly	His	Tyr	Ala	Arg	Thr	Asp	Tyr	Ala	Glu	Asn	Ala	
210					215					220						
Asn	Lys	Leu	Glu	Glu	Ser	Ala	Arg	Glu	His	His	Ile	Pro	Cys	Pro	Glu	
225					230					235					240	
His	Tyr	Asn	Gly	Phe	Cys	Met	His	Gly	Lys	Cys	Glu	His	Ser	Ile	Asn	
245					250					255						
Met	Gln	Glu	Pro	Ser	Cys	Arg	Cys	Asp	Ala	Gly	Tyr	Thr	Gly	Gln	His	
260					265					270						
Cys	Glu	Lys	Lys	Asp	Tyr	Ser	Val	Leu	Tyr	Val	Val	Pro	Gly	Pro	Val	
275					280					285						
Arg	Phe	Gln	Tyr	Val	Leu	Ile	Ala	Ala	Val	Ile	Gly	Thr	Ile	Gln	Ile	
290					295					300						
Ala	Val	Ile	Cys	Val	Val	Val	Leu	Cys	Ile	Thr	Arg	Lys	Cys	Pro	Arg	
305					310					315					320	
Ser	Asn	Arg	Ile	His	Arg	Gln	Lys	Gln	Asn	Thr	Gly	His	Tyr	Ser	Ser	
325					330					335						
Asp	Asn	Thr	Thr	Arg	Ala	Ser	Thr	Arg	Leu	Ile						
340					345											

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